	factors and hormones are well	described below under
	known in the art and may be	"Infectious Disease"). Highly
 	used or routinely modified to	preferred indications include
	assess the ability of	autoimmune diseases (e.g.,
 	polypeptides of the invention	rheumatoid arthritis, systemic
	(including antibodies and	lupus erythematosis, multiple
 	agonists or antagonists of the	sclerosis and/or as described
•	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
	differentiation and modulate T	described below). Highly
	cell proliferation and function.	preferred indications also
	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response
 ۹	evaluate the production of	and alternatively suppressing a
***	cytokines, such as IL-6, and	B cell-mediated immune
<i>p</i> c.	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
 	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
<u></u>	may be used or routinely	disorders.Additional highly
	modified to test	preferred indications include
 	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
 	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
-	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms

			approach" Chapter 6:138-160	and cancers, such as, myeloma,
-	···		(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
			Immunol 158:2919-2925	lymphoma, melanoma, and
			(1997), the contents of each of	prostate, breast, lung, colon,
-			which are herein incorporated	pancreatic, esophageal,
			by reference in its entirety.	stomach, brain, liver and
			Human dendritic cells that may	urinary cancer. Other preferred
			be used according to these	indications include benign
	_		assays may be isolated using	dysproliferative disorders and
	•		techniques disclosed herein or	pre-neoplastic conditions, such
			otherwise known in the art.	as, for example, hyperplasia,
			Human dendritic cells are	metaplasia, and/or dysplasia.
			antigen presenting cells in	Preferred indications include
			suspension culture, which,	anemia, pancytopenia,
			when activated by antigen	leukopenia, thrombocytopenia,
			and/or cytokines, initiate and	Hodgkin's disease, acute
			upregulate T cell proliferation	lymphocytic anemia (ALL),
			and functional activities.	multiple myeloma, Burkitt's
				lymphoma, arthritis, AIDS,
				granulomatous disease,
				inflammatory bowel disease,
				sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
		~-		reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
	_			meningitis, and Lyme Disease.
				An additonal preferred
	-			indication is infection (e.g., an

					infectious disease as described below under "Infectious Disease").
378	HHEPD24	1176	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
077				by T cells and has strong	embodiment of the invention
-				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
		•		IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
		***		has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic
				(including antibodies and	lupus erythematosis, multiple
				agonists or antagonists of the	sclerosis and/or as described
				invention) to mediate	below) and
				immunomodulation and	immunodeficiencies (e.g., as

		differentiation and modulate T	described below). Highly
		cell proliferation and function.	preferred indications also
		Exemplary assays that test for	include boosting a B cell-
	1.	immunomodulatory proteins	mediated immune response
		evaluate the production of	and alternatively suppressing a
	<u> </u>	cytokines, such as IL-6, and	B cell-mediated immune
	<u>t</u>	the stimulation and	response. Highly preferred
		upregulation of T cell	indications include
		proliferation and functional	inflammation and
		activities. Such assays that	inflammatory
		may be used or routinely	disorders. Additional highly
		modified to test	preferred indications include
		immunomodulatory and	asthma and allergy. Highly
		diffferentiation activity of	preferred indications include
		polypeptides of the invention	neoplastic diseases (e.g.,
		(including antibodies and	myeloma, plasmacytoma,
		agonists or antagonists of the	leukemia, lymphoma,
		invention) include assays	melanoma, and/or as described
		disclosed in Miraglia et al., J	below under
		Biomolecular Screening 4:193-	"Hyperproliferative
		204(1999); Rowland et al.,	Disorders"). Highly preferred
		"Lymphocytes: a practical	indications include neoplasms
		approach" Chapter 6:138-160	and cancers, such as, myeloma,
-		(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	I	Immunol 158:2919-2925	lymphoma, melanoma, and
		(1997), the contents of each of	prostate, breast, lung, colon,
	_	which are herein incorporated	pancreatic, esophageal,
		by reference in its entirety.	stomach, brain, liver and
	I	Human dendritic cells that may	urinary cancer. Other preferred
		be used according to these	indications include benign
	8	assays may be isolated using	dysproliferative disorders and

				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
	*				neutrophilia, psoriasis,
	***				suppression of immune
	-				reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
			-		meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
į					Disease").
	HHEPD24	1176	Production of	MCP-1 FMAT. Assays for	A highly preferred
228			MCP-1	immunomodulatory proteins	embodiment of the invention
				that are produced by a large	includes a method for
				variety of cells and act to	stimulating (e.g., increasing)
				induce chemotaxis and	MCP-1 production. An
				activation of monocytes and T	alternative highly preferred

cells are well known in the art	embodiment of the invention
and may be used or routinely	includes a method for
modified to assess the ability	. <u>S</u>
of polypeptides of the	MCP-1 production. A highly
invention (including antibodies	preferred indication is
and agonists or antagonists of	infection (e.g., an infectious
the invention) to mediate	disease as described below
immunomodulation, induce	under "Infectious Disease").
chemotaxis, and modulate	Additional highly preferred
immune cell activation.	indications include
Exemplary assays that test for	inflammation and
immunomodulatory proteins	inflammatory disorders.
evaluate the production of cell	Preferred indications include
surface markers, such as	blood disorders (e.g., as
monocyte chemoattractant	described below under
protein (MCP), and the	"Immune Activity", "Blood-
activation of monocytes and T	Related Disorders", and/or
cells. Such assays that may be	"Cardiovascular Disorders").
used or routinely modified to	Highly preferred indications
test immunomodulatory and	include autoimmune diseases
diffferentiation activity of	(e.g., rheumatoid arthritis,
polypeptides of the invention	systemic lupus erythematosis,
(including antibodies and	multiple sclerosis and/or as
agonists or antagonists of the	described below) and
invention) include assays	immunodeficiencies (e.g., as
disclosed in Miraglia et al., J	described below). Preferred
Biomolecular Screening 4:193-	indications also include
204(1999); Rowland et al.,	anemia, pancytopenia,
"Lymphocytes: a practical	leukopenia, thrombocytopenia,
approach" Chapter 6:138-160	Hodgkin's disease, acute
(2000); Satthaporn and	lymphocytic anemia (ALL),

plasmacytomas, multiple myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	y reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	r diabetes mellitus, endocarditis,	meningitis (bacterial and	viral), Lyme Disease, asthma,	and allergy Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,
Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and	Verhasselt et al., J Immunol	158:2919-2925 (1997), the	contents of each of which are	herein incorporated by	reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.												
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					metaplasia, and/or dysplasia.
	HHEPD24	1176	Production of	MIP-1alpha FMAT. Assays	A highly preferred
228		`	MIP1alpha	for immunomodulatory	embodiment of the invention
				proteins produced by activated	includes a method for
				dendritic cells that upregulate	stimulating MIP1a production.
				monocyte/macrophage and T	An alternative highly preferred
				cell chemotaxis are well	embodiment of the invention
	-	·		known in the art and may be	includes a method for
		•		used or routinely modified to	inhibiting (e.g., reducing)
				assess the ability of	MIP1a production. A highly
				polypeptides of the invention	preferred indication is
				(including antibodies and	infection (e.g., an infectious
	•			agonists or antagonists of the	disease as described below
-				invention) to mediate	under "Infectious Disease").
-				immunomodulation, modulate	Preferred indications include
				chemotaxis, and modulate T	blood disorders (e.g., as
				cell differentiation. Exemplary	described below under
				assays that test for	"Immune Activity", "Blood-
				immunomodulatory proteins	Related Disorders", and/or
<u>. </u>				evaluate the production of	"Cardiovascular Disorders").
				chemokines, such as	Highly preferred indications
				macrophage inflammatory	include autoimmune diseases
-				protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
				the activation of	systemic lupus erythematosis,
				monocytes/macrophages and T	multiple sclerosis and/or as
				cells. Such assays that may be	described below) and
	-			used or routinely modified to	immunodeficiencies (e.g., as
				test immunomodulatory and	described below). Additional
				chemotaxis activity of	highly preferred indications
				polypeptides of the invention	include inflammation and
				(including antibodies and	inflammatory disorders.

Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,		lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	asthma, and allergy.	Preferred indications also	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include
agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and	Eremin, J R Coll Surg Ednb	45(1):9-19 (2001); Drakes et	al., Transp Immunol 8(1):17-	29 (2000); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.	
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benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	a
	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or
	Production of TNF alpha by dendritic cells
	1176
	HHEPD24
	228

assays that may be used or	suppressing a T cell-mediated
routinely modified to test	immune response. Additional
immunomodulatory activity of	highly preferred indications
polypeptides of the invention	include inflammation and
(including antibodies and	inflammatory disorders, and
agonists or antagonists of the	treating joint damage in
invention) include assays	patients with rheumatoid
disclosed in Miraglia et al., J	arthritis. An additional highly
Biomolecular Screening 4:193-	preferred indication is sepsis.
204(1999); Rowland et al.,	Highly preferred indications
"Lymphocytes: a practical	include neoplastic diseases
approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
(2000); Verhasselt et al., Eur J	and/or as described below
Immunol 28(11):3886-3890	under "Hyperproliferative
(1198); Dahlen et al., J	Disorders"). Additionally,
Immunol 160(7):3585-3593	highly preferred indications
(1998); Verhasselt et al., J	include neoplasms and
Immunol 158:2919-2925	cancers, such as, leukemia,
(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
(1999), the contents of each of	tumors, and prostate, breast,
which are herein incorporated	lung, colon, pancreatic,
by reference in its entirety.	esophageal, stomach, brain,
Human dendritic cells that may	liver and urinary cancer. Other
be used according to these	preferred indications include
 assays may be isolated using	benign dysproliferative
techniques disclosed herein or	disorders and pre-neoplastic
otherwise known in the art.	conditions, such as, for
Human dendritic cells are	example, hyperplasia,
antigen presenting cells in	metaplasia, and/or dysplasia.
suspension culture, which,	Preferred indications include

			``	when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation.
					diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below under "Infectious Disease").
229	HHEPM33	1177	SEAP in 293/ISRE		
229	ННЕРМ33	1177	Activation of transcription	Assays for the activation of transcription through the	A highly preferred indication is obesity and/or complications
			through cAMP response element	cAMP response element are well-known in the art and may	associated with obesity. Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred

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	indication is diabetes mellitus.	An additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the		section below), dyslipidemia,	endocrine disorders (as
	(including antibodies and	agonists or antagonists of the	invention) to increase cAMP,	regulate CREB transcription	factors, and modulate	expression of genes involved	in a wide variety of cell	functions. For example, a	3T3-L1/CRE reporter assay	may be used to identify factors	that activate the cAMP	signaling pathway. CREB	plays a major role in	adipogenesis, and is involved	in differentiation into	adipocytes. CRE contains the	binding sequence for the	transcription factor CREB	(CRE binding protein).	Exemplary assays for	transcription through the	cAMP response element that	may be used or routinely	modified to test cAMP-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and
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				7,0 =																											

		į		Malm, Methods in Enzymol	described in the "Endocrine
				216:362-368 (1992); Henthorn	Disorders" section below),
				et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
				85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
				et al., Mol Cell Biol	blindness), ulcers and impaired
				20(3):1008-1020 (2000); and	wound healing, and infection
				Klemm et al., J Biol Chem	(e.g., infectious diseases and
				273:917-923 (1998), the	disorders as described in the
				contents of each of which are	"Infectious Diseases" section
				herein incorporated by	below, especially of the
				reference in its entirety. Pre-	urinary tract and skin), carpal
				adipocytes that may be used	tunnel syndrome and
				according to these assays are	Dupuytren's contracture).
				publicly available (e.g.,	Additional highly preferred
				through the ATCC) and/or	indications are complications
				may be routinely generated.	associated with insulin
				Exemplary mouse adipocyte	resistance.
				cells that may be used	
				according to these assays	
				include 3T3-L1 cells. 3T3-L1	
				is an adherent mouse	
				preadipocyte cell line that is a	
				continuous substrain of 3T3	
				fibroblast cells developed	
,				through clonal isolation and	
		-		undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				conditions known in the art.	
1	HHEPM33	1177	Activation of	This reporter assay measures	Highly preferred indications
229			transcription	activation of the GATA-3	include allergy, asthma, and

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rhinitis Additional preferred	indications include infection	(e.g., an infectious disease as	low under	"Infectious Disease"), and	n and	y disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described		immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	., leukemia,	nelanoma,	prostate, breast, lung, colon,	sophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	low under	erative	Disorders"). Other preferred
rhinitis Ado	indications in	e.g., an infe	described below under	"Infectious I	inflammation and	inflammatory disorders.	Preferred inc	include bloo	as described	"Immune Ac	Related Diso	"Cardiovascu	Preferred ind	autoimmune	rheumatoid a	lupus eryther	sclerosis and	below) and	immunodefic	described be	indications in	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, brea	pancreatic, esophageal,	stomach, bra	urinary tract	described below under	"Hyperproliferative	Disorders").
signaling pathway in HMC-1	human mast cell line.	Activation of GATA-3 in mast	cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription	through the GATA3 response	element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate GATA3 transcription	factors and modulate	expression of mast cell genes	important for immune response	development. Exemplary	assays for transcription	through the GATA3 response	element that may be used or	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and
signalii			cells h	cytokir	produc	activati	through	elemen	art and	routine	the abil	the inv	antibod	antagor	regulat	factors	express	importa	develor	assays	through	elemen	routine	GATA	activity	inventi	and ago	the inve	disclose	66:1-10
through GATA-3	response element in	immune cells (such	as mast cells).																											
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				Malm. Methods in Enzymol	indications include henign
				216:362-368 (1992): Henthorn	dysproliferative disorders and
				et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
				85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
				et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
				Quant Biol 64:563-571 (1999);	Preferred indications include
-				Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
				J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
				(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
				Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
				Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
		•		Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
	,			cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HHEPM33	1177	Activation of	This reporter assay measures	Highly preferred indications
229			transcription	activation of the NFAT	include allergy, asthma, and

rhinitis. Additional preferred indications include infection	(e.g., an infectious disease as	described below under	"Infectious Disease"), and	inflammation and	inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred
signaling pathway in HMC-1 human mast cell line.	Activation of NFAT in mast	cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription	through the Nuclear Factor of	Activated T cells (NFAT)	response element are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays
through NFAT response element in	immune cells (such	as mast cells).									•			-			<i>3</i>				-								
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									3.00																•				

	disclosed	in Berger et al., Gene	disclosed in Berger et al., Gene indications include benign
	66:1-10 (66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, M	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-3	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Pro	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6	85:6342-6346 (1988); De Boer	Preferred indications include
	et al., Int	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):12	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et al., J Immunol	nmunol	leukemias, Hodgkin's disease,
	165(12):7	165(12):7215-7223 (2000);	acute lymphocytic anemia
	Hutchinsc	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
-	Biol Cher	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
	16338 (19	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
	al., J Exp	al., J Exp Med 188:527-537	granulomatous disease,
	(1998), th	(1998), the contents of each of	inflammatory bowel disease,
	which are	which are herein incorporated	sepsis, neutropenia,
	by referer	by reference in its entirety.	neutrophilia, psoriasis,
	Mast cells	Mast cells that may be used	suppression of immune
-	according	according to these assays are	reactions to transplanted
	publicly a	publicly available (e.g.,	organs and tissues, hemophilia,
	through th	through the ATCC).	hypercoagulation, diabetes
	Exemplar	Exemplary human mast cells	mellitus, endocarditis,
	that may	that may be used according to	meningitis, and Lyme Disease.
	these assa	these assays include the HMC-	
	1 cell line	1 cell line, which is an	
	immature	immature human mast cell line	
	establishe	established from the peripheral	
	s to boold	blood of a patient with mast	
	cell leuke	cell leukemia, and exhibits	
	many cha	many characteristics of	
	immature	immature mast cells.	

	HHEPM33	1177	Activation of	Assays for the activation of	Highly preferred indications
229			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response element in	cells (NFAT) response element	"Immune Activity", "Blood-
			immune cells (such	are well-known in the art and	Related Disorders", and/or
			as natural killer	may be used or routinely	"Cardiovascular Disorders").
<u>-</u>			cells).	modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
·				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An
				polypeptides of the invention	additional highly preferred
				(including antibodies and	indication is infection (e.g., an
				agonists or antagonists of the	infectious disease as described
				invention) include assays	below under "Infectious
				disclosed in Berger et al., Gene	Disease"). Preferred
				66:1-10 (1998); Cullen and	indications include neoplastic
				Malm, Methods in Enzymol	diseases (e.g., leukemia,
				216:362-368 (1992); Henthorn	lymphoma, and/or as described
				et al., Proc Natl Acad Sci USA	below under
				85:6342-6346 (1988);	"Hyperproliferative

Disorders"). Preferred indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	and prostate, breast, lung,	colon, pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	asthma and allergy.
Aramburu et al., J Exp Med 182(3):801-810 (1995); De	Boer et al., Int J Biochem Cell	Biol 31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. NK	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human NK cells	that may be used according to	these assays include the NK-	YT cell line, which is a human	natural killer cell line with	cytolytic and cytotoxic	activity.									
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A preferred embodiment of	the invention includes a	method for inhibiting (e.g.,	reducing) TNF alpha	production. An alternative	highly preferred embodiment	of the invention includes a	method for stimulating (e.g.,	increasing) TNF alpha	production. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies				suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and
Assays for the activation of	transcription through the	Serum Response Element	(SRE) are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate serum response	factors and modulate the	expression of genes involved	in growth and upregulate the	function of growth-related	genes in many cell types.	Exemplary assays for	transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-
Activation of	transcription	through serum	response element in	immune cells (such	as natural killer	cells).																								
1177																														
ННЕРМ33																														
	229						_								15		-													

treating joint damage in patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),
3873 (1994); and Black et al., Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.					-											
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					piasiliacytolilas, munipie
					myeloma, Burkitt's lymphoma,
-					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HHEPM33	1177	SEAP in		
229			NK16/STAT6		
	HHEPM33	1177	Hexosaminidase in		
229			RBL-2H3		
	HHEPM33	1177	Activation of	Assays for the activation of	Highly preferred indications
229			transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
			response element in	Site (GAS) response element	and/or as described below
			immune cells (such	are well-known in the art and	under "Hyperproliferative
	18.5		as T-cells).	may be used or routinely	Disorders"). Highly preferred
				modified to assess the ability	indications include neoplasms
				of polypeptides of the	and cancers, such as, for
				invention (including antibodies	example, leukemia, lymphoma

and ag	and agonists or antagonists of	(e.g., T cell lymphoma,
the in	the invention) to regulate	Burkitt's lymphoma, non-
STAT	STAT transcription factors and	Hodgkins lymphoma,
npom	modulate gene expression	Hodgkin"s disease),
Novai	involved in a wide variety of	melanoma, and prostate,
cell fu	cell functions. Exemplary	breast, lung, colon, pancreatic,
assays	assays for transcription	esophageal, stomach, brain,
throug	through the GAS response	liver and urinary cancer. Other
eleme	element that may be used or	preferred indications include
routin	routinely modified to test	benign dysproliferative
GAS	GAS-response element activity	disorders and pre-neoplastic
lod bo	of polypeptides of the	conditions, such as, for
invent	invention (including antibodies	example, hyperplasia,
and ag	and agonists or antagonists of	metaplasia, and/or dysplasia.
the inv	the invention) include assays	Preferred indications include
disclo	disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
66:1-1	66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
Malm	Malm, Methods in Enzymol	lupus erythematosis, multiple
216:3	216:362-368 (1992); Henthorn	sclerosis and/or as described
et al.,	et al., Proc Natl Acad Sci USA	below), immunodeficiencies
85:63	85:6342-6346 (1988);	(e.g., as described below),
Matik	Matikainen et al., Blood	boosting a T cell-mediated
93(6):	93(6):1980-1991 (1999); and	immune response, and
Hentti	Henttinen et al., J Immunol	suppressing a T cell-mediated
155(1)	155(10):4582-4587 (1995), the	immune response. Additional
conter	contents of each of which are	preferred indications include
herein	herein incorporated by	inflammation and
refere	reference in its entirety.	inflammatory disorders.
Exem		Highly preferred indications
such a	such as the SUPT cell line, that	include blood disorders (e.g.,
may b	may be used according to these	as described below under

	chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional	preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia	(ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,	suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allerey.
assays are publicly available (e.g., through the ATCC).				

	HHEPT60	1178	Activation of	Assays for the activation of	Highly preferred indications
230			transcription	transcription through the	include inflammation and
	-		through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
71			as natural killer	to assess the ability of	as described below under
			cells).	polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
	-			invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
				NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications
				disclosed in Berger et al., Gene	include neoplastic diseases
				66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
				Malm, Methods in Enzymol	lymphoma, and/or as described
				216:362-368 (1992); Henthorn	below under
				et al., Proc Natl Acad Sci USA	"Hyperproliferative
			-	85:6342-6346 (1988); Valle	Disorders"). Highly preferred
				Blazquez et al, Immunology	indications include neoplasms
				90(3):455-460 (1997);	and cancers, such as, for

				Aramburau et al J Exp Med	example, melanoma, renal cell
				82(3):801-810 (1995): and	carcinoma lenkemia
				Fraser et al., 29(3):838-844	lymphoma, and prostate.
				(1999), the contents of each of	breast, lung, colon, pancreatic,
				which are herein incorporated	esophageal, stomach, brain,
				by reference in its entirety.	liver and urinary cancer. Other
				NK cells that may be used	preferred indications include
	,			according to these assays are	benign dysproliferative
				publicly available (e.g.,	disorders and pre-neoplastic
				through the ATCC).	conditions, such as, for
				Exemplary human NK cells	example, hyperplasia,
				that may be used according to	metaplasia, and/or dysplasia.
				these assays include the NKL	Preferred indications also
				cell line, which is a human	include anemia, pancytopenia,
				natural killer cell line	leukopenia, thrombocytopenia,
				established from the peripheral	Hodgkin's disease, acute
				blood of a patient with large	lymphocytic anemia (ALL),
				granular lymphocytic	plasmacytomas, multiple
				leukemia. This IL-2 dependent	myeloma, Burkitt's lymphoma,
				suspension culture cell line has	arthritis, AIDS, granulomatous
				a morphology resembling that	disease, inflammatory bowel
				of activated NK cells.	disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
-					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
	HHEPU04	1179	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
231				by T cells and has strong	embodiment of the invention

effects on B cells. IL-6
participates in IL-4 induced
IgE production and increases
IgA production (IgA plays a
role in mucosal immunity).
IL-6 induces cytotoxic T cells.
Deregulated expression of IL-6
has been linked to autoimmune
disease, plasmacytomas,
myelomas, and chronic
hyperproliferative diseases.
Assays for immunomodulatory
and differentiation factor
proteins produced by a large
variety of cells where the
expression level is strongly
regulated by cytokines, growth
factors, and hormones are well
known in the art and may be
used or routinely modified to
assess the ability of
polypeptides of the invention
(including antibodies and
agonists or antagonists of the
invention) to mediate
immunomodulation and
differentiation and modulate T
cell proliferation and function.
Exemplary assays that test for
immunomodulatory proteins
evaluate the production of

	cytokines, such as IL-6, and	B cell-mediated immune
	the stimulation and upregulation of T cell	response. Highly preferred indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
	may be used or routinely	disorders. Additional highly
	modified to test	preferred indications include
	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
-	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
 	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
	Human dendritic cells that may	urinary cancer. Other preferred
	be used according to these	indications include benign
	assays may be isolated using	dysproliferative disorders and
	techniques disclosed herein or	pre-neoplastic conditions, such
	otherwise known in the art.	as, for example, hyperplasia,
	Human dendritic cells are	metaplasia, and/or dysplasia.
	antigen presenting cells in	Preferred indications include
	suspension culture, which,	anemia, pancytopenia,

				when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities	leukopenia, thrombocytopenia, Hodgkin's disease, acute Iymphocytic anemia (ALL), multiple myeloma, Burkitt's
				aliu iulicuoliai activitics.	lymphoma, arthritis, AIDS, granulomatous disease,
					inflammatory bowel disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HHEPU04	1179	Production of TNF	TNFa FMAT. Assays for	A highly preferred
231			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred
	-			wide variety of inflammatory	embodiment of the invention
				and cytotoxic effects on a	includes a method for
				variety of cells are well known	stimulating (e.g., increasing)
				in the art and may be used or	TNF alpha production.
				routinely modified to assess	Highly preferred indications

	the ahi	the ability of nolynentides of	include blood disorders (e o
	vii ett	the invention (including	as described helow under
		Cinton (mending	as described below under
	antiboc	antibodies and agonists or	"Immune Activity", "Blood-
	antago	antagonists of the invention) to	Related Disorders", and/or
	mediat	mediate immunomodulation,	"Cardiovascular Disorders"),
	modul	modulate inflammation and	Highly preferred indications
	cytotox	cytotoxicity. Exemplary	include autoimmune diseases
-	assays	assays that test for	(e.g., rheumatoid arthritis,
	immun	immunomodulatory proteins	systemic lupus erythematosis,
	evaluat	evaluate the production of	Crohn"s disease, multiple
	cytokir	cytokines such as tumor	sclerosis and/or as described
	necrosi	necrosis factor alpha (TNFa),	below), immunodeficiencies
	and the	and the induction or inhibition	(e.g., as described below),
,	of an ii	of an inflammatory or	boosting a T cell-mediated
	cytoto	cytotoxic response. Such	immune response, and
	assays	assays that may be used or	suppressing a T cell-mediated
	routine	routinely modified to test	immune response. Additional
	immun	immunomodulatory activity of	highly preferred indications
	polype	polypeptides of the invention	include inflammation and
	(includ	(including antibodies and	inflammatory disorders, and
	agonist	agonists or antagonists of the	treating joint damage in
	inventi	invention) include assays	patients with rheumatoid
	disclos	disclosed in Miraglia et al., J	arthritis. An additional highly
	Biomo	Biomolecular Screening 4:193-	preferred indication is sepsis.
	204(19	204(1999); Rowland et al.,	Highly preferred indications
	"Lymb	"Lymphocytes: a practical	include neoplastic diseases
	approa	approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
	(2000)	(2000); Verhasselt et al., Eur J	and/or as described below
	Immur	Immunol 28(11):3886-3890	under "Hyperproliferative
	(1198)	(1198); Dahlen et al., J	Disorders"). Additionally,
	Immur	Immunol 160(7):3585-3593	highly preferred indications

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include neoplasms and cancers, such as, leukemia,	lymphoma, melanoma, giloma (e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,
(1998); Verhasselt et al., J Immunol 158:2919-2925	(1997); and Nardelli et al., J Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.												
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													-															

described below under "Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or cardiovascularization. Highly
	Disc	the	(e.g	hear	aort	carc	regr	dysi	and	dise	intr	hyp	infa	hen	as d	"Ca	Hig	incl	end	disc	disc	snc	wel	the	arte	and	pre	stin

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preferred are indications that	inhibit angiogenesis and/or	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.
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		_																							-				

Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s	phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as	wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke,

graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders,	age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred	heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include	blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such inflammatory disorders (such
			,		

function, and/or mediate	lupus erythematosis, multiple
humoral or cell-mediated	sclerosis and/or as described
 immunity. Exemplary assays	below), immunodeficiency
 that test for	(e.g., as described below),
 immunomodulatory proteins	boosting a T cell-mediated
evaluate the production of	immune response, and
cytokines, such as Interferon	suppressing a T cell-mediated
gamma (IFNg), and the	immune response. Additional
activation of T cells. Such	highly preferred indications
assays that may be used or	include inflammation and
 routinely modified to test	inflammatory disorders.
immunomodulatory activity of	Additional preferred
polypeptides of the invention	indications include idiopathic
(including antibodies and	pulmonary fibrosis. Highly
agonists or antagonists of the	preferred indications include
invention) include the assays	neoplastic diseases (e.g.,
disclosed in Miraglia et al., J	leukemia, lymphoma,
Biomolecular Screening 4:193-	
204 (1999); Rowland et al.,	below under
 "Lymphocytes: a practical	"Hyperproliferative
approach" Chapter 6:138-160	Disorders"). Highly preferred
(2000); Gonzalez et al., J Clin	indications include neoplasms
 Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
15:749-795 (1997), and	esophageal, stomach, brain,
Rheumatology (Oxford)	liver and urinary cancer. Other
38(3):214-20 (1999), the	preferred indications include
contents of each of which are	benign dysproliferative
herein incorporated by	disorders and pre-neoplastic

				reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia pancytopenia
				otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple
				express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-	myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel
				mediated immunity and may be preactivated to enhance	disease, sepsis, neutropenia, neutrophilia, psoriasis,
				responsiveness to immunomodulatory factors.	suppression of immune reactions to transplanted
					organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,
	HHFFI48	1182	Activation of	Kinase assav. Kinase assavs.	asthma and allergy. A highly preferred
234			Adipocyte PI3 Kinase Signalling	for example an GSK-3 assays, for PI3 kinase signal	embodiment of the invention includes a method for
	-		Pathway	transduction that regulate glucose metabolism and cell	increasing adipocyte survival An alternative highly preferred
				survival are well-known in the art and may be used or	embodiment of the invention includes a method for
				routinely modified to assess	decreasing adipocyte survival.
				the ability of polypeptides of the invention (including	A preferred embodiment of the invention includes a method

	ne	antihodies and agonists or	for stimulating adinocyte
		to conict of the invention) to	moliforation An alternative
		antagonists of the invention) to	pioliferation. An ancinative
	ud	promote or inhibit glucose	highly preferred embodiment
	m	metabolism and cell survival.	of the invention includes a
	<u>B</u>	Exemplary assays for PI3	method for inhibiting
	<u> </u>	kinase activity that may be	adipocyte proliferation. A
	sn	used or routinely modified to	preferred embodiment of the
	te	test PI3 kinase-induced activity	invention includes a method
	Jo	of polypeptides of the	for stimulating adipocyte
	<u>ii</u>	invention (including antibodies	differentiation. An alternative
	an	and agonists or antagonists of	highly preferred embodiment
		the invention) include assays	of the invention includes a
	di di	disclosed in Forrer et al., Biol	method for inhibiting
	<u>5</u>	Chem 379(8-9):1101-1110	adipocyte differentiation.
	1)	(1998); Nikoulina et al.,	Highly preferred indications
	<u> </u>	Diabetes 49(2):263-271	include endocrine disorders
	(2	(2000); and Schreyer et al.,	(e.g., as described below under
	<u>D</u>	Diabetes 48(8):1662-1666	"Endocrine Disorders").
	1)	(1999), the contents of each of	Preferred indications include
		which are herein incorporated	neoplastic diseases (e.g.,
		by reference in its entirety.	lipomas, liposarcomas, and/or
	$\overline{\mathbb{Z}}$	Mouse adipocyte cells that	as described below under
	 	may be used according to these	"Hyperproliferative
_	as	assays are publicly available	Disorders"), blood disorders
	<u>(e</u>	(e.g., through the ATCC).	(e.g., hypertension, congestive
		Exemplary mouse adipocyte	heart failure, blood vessel
	90	cells that may be used	blockage, heart disease, stroke,
	ac	according to these assays	impotence and/or as described
	ni	include 3T3-L1 cells. 3T3-L1	below under "Immune
	si	is an adherent mouse	Activity", "Cardiovascular
	rd	preadipocyte cell line that is a	Disorders", and/or "Blood-

Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under		ndicat	diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease	(e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal	Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy),	disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness,
continous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under	appropriate differentiation conditions known in the art.			·	-	

nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease,	hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as	described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below especially of the	urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight loss or alternatively,

highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Highly preferred	indications include neoplasms	and cancer, such as, lipoma,	liposarcoma, lymphoma,	leukemia and breast, colon,	and kidney cancer. Additional	highly preferred indications	include melanoma, prostate,	lung, pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such
				-														-					•							

as, for example, hyperplasia, metaplasia, and/or dysplasia.		Assays for A highly preferred	s em	ed by a large includes a method for	and act to stimulating (e.g., increasing)					ess the ability inhibiting (e.g., reducing)		preferred indication is	antagonists of infection (e.g., an infectious			I modulate Additional highly preferred			tory proteins inflammatory disorders.	duction of cell Preferred indications include	such as blood disorders (e.g., as	oattractant described below under		onocytes and T Related Disorders", and/or		y modified to Highly preferred indications		
	k Phos	of MCP-1 FMAT. Assays for	immunomodulatory proteins	that are produced by a large	variety of cells and act to	induce chemotaxis and	activation of monocytes and T	cells are well known in the art	and may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to mediate	immunomodulation, induce	chemotaxis, and modulate	immune cell activation.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of cell	surface markers, such as	monocyte chemoattractant	protein (MCP), and the	activation of monocytes and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	J: 7: 7: 7: 7: 7: 7: 7: 7: 7: 7: 7: 7: 7:
	SEAP in Alk Phos C2C12	Production of	MCP-1			-																				- 19		
	HHFGR93 11	HHFGR93 11	•											-											-			
	235		235																									

(including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and functional activities.

and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Wound Healing, and Inflamation. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal,
	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of epithhelial genes. Exemplary assays for transcription through the NFKB response element that may be used or routinely modified to test NFKB-response element activity of polypeptides of the invention (including cartification) and including cartified in the in
	Activation of transcription through NFKB response element in epithelial cells (such as HELA cells).
	1183
	HHFGR93
	235

urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include inflammatory disorders. inflammatory disorders.		
and agonists or antagonists of the invention) include assays disclosed in: Kaltschmidt B, et al., Oncogene, 18(21):3213-3225 (1999); Beetz A, et al., Int J Radiat Biol, 76(11):1443-1453 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Epithelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary epithelial cells that may be used according to these assays include the HELA cell	line.	
	IFNg in Human T-	cell 2B9
	1183	
	HHFGR93	
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RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and	eosinophils are well known in the art and may be used or routinely modified to assess	the ability of polypeptides of the invention (including	antibodies and agonists or antagonists of the invention) to	mediate immunomodulation, induce chemotaxis, and/or	mediate humoral or cell-	mediated immunity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as KAN I ES, and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-
Production of RANTES in bronchial epithelium cells	•				,,,-		_														
1183						-															
HHFGR93																					
235																					

	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Infection, Inflammation, Atherosclerosis, Hypersensitivity, and Leukemias
204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000): Cocchi et al., Science 270(5243):1811-1815 (1995); and Robinson et al., Clin Exp Immunol 101(3):398-407 (1995), the contents of each of which are herein incorporated by reference in its entirety. Epithelial cells were isolated from bronchia/trachea immediately postmortem from humans who were free of known respiratory diseases. See Wu et al., Am Rev Respir Dis. 132(2):311-20 (1985), the contents of which are herein incorporated by reference in its entirety.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. Cells normally have very low concentrations of cytosolic calcium compared to
	Calcium flux in immune cells (such as monocytes)
	1183
	HHFGR93
1551	235

much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary	assays that may be used or routinely modified to measure calcium flux in immune cells (such as monocytes) include assays disclosed in: Chan, CC, et al., J Pharmacol Exp Ther, 269(3):891-896 (1994);	Andersson, K, et al., Cytokine, 12(12):1784-1787 (2000); Scully, SP, et al., J Clin Invest, 74(2) 589-599 (1984); and, Sullivan, E, et al., Methods Mol Biol, 114:125-133 (1999), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to	these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the THP-1 monocyte

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			A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A
contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays	include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6.	differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6
			Production of IL-6
			1185
			HHFHR32
			237

		has been linked to autoimmune	highly preferred indication is
			the stimulation or enhancement
		myelomas, and chronic	of mucosal immunity. Highly
		hyperproliferative diseases.	preferred indications include
		Assays for immunomodulatory	blood disorders (e.g., as
		and differentiation factor	described below under
		proteins produced by a large	"Immune Activity", "Blood-
		variety of cells where the	Related Disorders", and/or
	-	expression level is strongly	"Cardiovascular Disorders"),
		regulated by cytokines, growth	and infection (e.g., as
		factors, and hormones are well	described below under
		known in the art and may be	"Infectious Disease"). Highly
		used or routinely modified to	preferred indications include
		assess the ability of	autoimmune diseases (e.g.,
		polypeptides of the invention	rheumatoid arthritis, systemic
,		(including antibodies and	lupus erythematosis, multiple
		agonists or antagonists of the	sclerosis and/or as described
		invention) to mediate	below) and
		immunomodulation and	immunodeficiencies (e.g., as
		differentiation and modulate T	described below). Highly
		cell proliferation and function.	preferred indications also
		Exemplary assays that test for	include boosting a B cell-
		immunomodulatory proteins	mediated immune response
		evaluate the production of	and alternatively suppressing a
	 -	cytokines, such as IL-6, and	B cell-mediated immune
		the stimulation and	response. Highly preferred
		upregulation of T cell	indications include
		proliferation and functional	inflammation and
		activities. Such assays that	inflammatory
		may be used or routinely	disorders. Additional highly
		modified to test	preferred indications include

asthma and allergy. Highly preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma,	leukemia, lymphoma, melanoma, and/or as described below under "Hynernroliferative	Disorders"). Highly preferred indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia,	lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and		pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute	lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,
immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193.	204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160	Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety	Human dendritic cells that may be used according to these assays may be isolated using	techniques disclosed herein or otherwise known in the art. Human dendritic cells are	antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and	upregulate T cell proliferation and functional activities.
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sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative highly preferred embodiment of the invention
		Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation.
	SEAP in Jurkat/IL4 promoter (antiCD3 co-stim)	Activation of Natural Killer Cell ERK Signaling Pathway.
	1186	1186
	HHF0J29	HHF0J29
	238	238

kinase activity that may be	includes a method for
section of the different control of	1.0 1.1.1.1.2
used or routinely modified to	# X
test ERK kinase-induced	differentiation. Highly
activity of polypeptides of the	preferred indications include
invention (including antibodies	neoplastic diseases (e.g., as
and agonists or antagonists of	described below under
the invention) include the	"Hyperproliferative
assays disclosed in Forrer et	Disorders"), blood disorders
al., Biol Chem 379(8-9):1101-	(e.g., as described below under
1110 (1998); Kyriakis JM,	"Immune Activity",
Biochem Soc Symp 64:29-48	"Cardiovascular Disorders",
(1999); Chang and Karin,	and/or "Blood-Related
 Nature 410(6824):37-40	Disorders"), immune disorders
(2001); and Cobb MH, Prog	(e.g., as described below under
Biophys Mol Biol 71(3-4):479-	"Immune Activity") and
500 (1999); the contents of	infections (e.g., as described
 each of which are herein	below under "Infectious
 incorporated by reference in its	Disease"). Preferred
entirety. Natural killer cells	indications include blood
that may be used according to	disorders (e.g., as described
 these assays are publicly	below under "Immune
available (e.g., through the	Activity", "Blood-Related
ATCC). Exemplary natural	Disorders", and/or
 killer cells that may be used	"Cardiovascular Disorders").
according to these assays	Highly preferred indications
 include the human natural	include autoimmune diseases
killer cell lines (for example,	(e.g., rheumatoid arthritis,
NK-YT cells which have	systemic lupus erythematosis,
cytolytic and cytotoxic	multiple sclerosis and/or as
activity) or primary NK cells.	described below) and
	immunodeficiencies (e.g., as

described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include cancers such as,	kidney, melanoma, prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary cancer,	lymphoma and leukemias.	Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Other highly preferred	indications include,	pancytopenia, leukopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), arthritis, asthma,	AIDS, granulomatous disease,	inflammatory bowel disease,	sepsis, psoriasis, immune	reactions to transplanted	organs and tissues,	endocarditis, meningitis, Lyme	Disease, and allergies.	A highly preferred
																														Kinase assay. Kinase assays,
																														Kinase assay.
																														Activation of
																									* 40***********************************					1187
																							-				٠			HHGBO91
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embodiment of the invention includes a method for stimulating adipocyte	highly preferred embodiment of the invention includes a method for inhibiting	adipocyte proliferation. A highly preferred embodiment of the invention includes a	method for stimulating adipocyte differentiation. An	alternative highly preferred embodiment of the invention	includes a method for inhibiting adipocyte	differentiation. A highly	preferred embodiment of the invention includes a method	for stimulating (e.g.,	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	acuvation of (e.g., decreasing) and/or inactivating adinocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").
for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation.	are well known in the art and may be used or routinely modified to assess the ability	of polypeptides of the invention (including antibodies and agonists or antagonists of	the invention) to promote or inhibit cell proliferation,	activation, and differentiation. Exemplary assays for ERK	kinase activity that may be used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and
Adipocyte ERK Signaling Pathway																	
								-					• •			*****	
239					154							i					

Cobb MH, Prog Biophys Mol	Highly preferred indications
Biol 71(3-4):479-500 (1999);	also include neoplastic
the contents of each of which	diseases (e.g., lipomas,
are herein incorporated by	liposarcomas, and/or as
reference in its entirety.	described below under
Mouse adipocyte cells that	"Hyperproliferative
may be used according to these	
assays are publicly available	indications include blood
(e.g., through the ATCC).	disorders (e.g., hypertension,
Exemplary mouse adipocyte	congestive heart failure, blood
cells that may be used	vessel blockage, heart disease,
according to these assays	stroke, impotence and/or as
include 3T3-L1 cells. 3T3-L1	described below under
is an adherent mouse	"Immune Activity",
preadipocyte cell line that is a	"Cardiovascular Disorders",
continuous substrain of 3T3	and/or "Blood-Related
fibroblast cells developed	Disorders"), immune disorders
through clonal isolation and	(e.g., as described below under
undergo a pre-adipocyte to	"Immune Activity"), neural
adipose-like conversion under	disorders (e.g., as described
appropriate differentiation	below under "Neural Activity
conditions known in the art.	and Neurological Diseases"),
	and infection (e.g., as
	described below under
	"Infectious Disease").
	A highly preferred indication
	is diabetes mellitus. An
	additional highly preferred
	indication is a complication
	associated with diabetes (e.g.,
	diabetic retinopathy, diabetic

nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired
										-																				

wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems	muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, and kidney diseases or disorders. Preferred

indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.		A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below),
ind and lyn bre can ind ind pro eso eso live lipe ind dys pre eso eso eso eso eso eso eso eso eso es		Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion dis measured by FMAT using detainsulin antibodies. Dianagement
	IL-10 in Human T- cell 293T	Stimulation of Assainsulin secretion of instinction pancreatic the arbeta cells. Touting the arbeta cells. The arbeta cells antiper antiper antiper antiper antiper antiper antiper antiper stimuling the arbeta cells.
	1188	1188
	HHGCM76	HHGCM76
	240	240

		Insulin secretion from	diabetic neuropathy, nerve
		pancreatic beta cells is	disease and nerve damage
		upregulated by glucose and	(e.g., due to diabetic
		also by certain	neuropathy), blood vessel
		proteins/peptides, and	blockage, heart disease, stroke,
		disregulation is a key	impotence (e.g., due to diabetic
		component in diabetes.	neuropathy or blood vessel
		Exemplary assays that may be	blockage), seizures, mental
		used or routinely modified to	confusion, drowsiness,
		test for stimulation of insulin	nonketotic hyperglycemic-
		secretion (from pancreatic	hyperosmolar coma,
		cells) by polypeptides of the	cardiovascular disease (e.g.,
		invention (including antibodies	heart disease, atherosclerosis,
		and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
		disclosed in: Ahren, B., et al.,	diseases and disorders as
		Am J Physiol, 277(4 Pt	described in the
		2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
-		al., Endocrinology,	section below), dyslipidemia,
		138(9):3735-40 (1997); Kim,	endocrine disorders (as
		K.H., et al., FEBS Lett,	described in the "Endocrine
	11-	377(2):237-9 (1995); and,	Disorders" section below),
		Miraglia S et. al., Journal of	neuropathy, vision impairment
		Biomolecular Screening,	(e.g., diabetic retinopathy and
		 4:193-204 (1999), the contents	blindness), ulcers and impaired
	-	of each of which is herein	wound healing, and infection
		incorporated by reference in its	(e.g., infectious diseases and
		entirety. Pancreatic cells that	disorders as described in the
		may be used according to these	"Infectious Diseases" section
		assays are publicly available	below, especially of the
		(e.g., through the ATCC)	urinary tract and skin), carpal

tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281
	Production of ICAM-1
	1188
	HHGCM76
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	— Т												-				\neg
		A highly preferred	includes a method for	stimulating adipocyte	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	adipocyte proliferation. A	highly preferred embodiment	of the invention includes a	method for stimulating	adipocyte differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting adipocyte
(2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays	include microvascular endothelial cells (MVEC).	Kinase assay. Kinase assays,	for example an EIK-1 kinase	assay, 101 ENN signal transduction that regulate cell	proliferation or differentiation	are well known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to
		Activation of	Adipocyte EKK	Signaling Fathway													
		1189															
		HHGCQ54															
			241														

	test ERK kinase-induced	differentiation. A highly
	activity of polypeptides of the	preferred embodiment of the
	invention (including antibodies	invention includes a method
	and agonists or antagonists of	for stimulating (e.g.,
1000	 the invention) include the	increasing) adipocyte
	assays disclosed in Forrer et	activation. An alternative
 	al., Biol Chem 379(8-9):1101-	highly preferred embodiment
 	1110 (1998); Le Marchand-	of the invention includes a
 	Brustel Y, Exp Clin	method for inhibiting the
 	 Endocrinol Diabetes	activation of (e.g., decreasing)
 	107(2):126-132 (1999);	and/or inactivating adipocytes.
 ***	Kyriakis JM, Biochem Soc	Highly preferred indications
 	Symp 64:29-48 (1999); Chang	include endocrine disorders
 	 and Karin, Nature	(e.g., as described below under
 	 410(6824):37-40 (2001); and	"Endocrine Disorders").
 	 Cobb MH, Prog Biophys Mol	Highly preferred indications
	Biol 71(3-4):479-500 (1999);	also include neoplastic
 	the contents of each of which	diseases (e.g., lipomas,
 	 are herein incorporated by	liposarcomas, and/or as
	 reference in its entirety.	described below under
 	 Mouse adipocyte cells that	"Hyperproliferative
	 may be used according to these	Disorders"). Preferred
	 assays are publicly available	indications include blood
 	 (e.g., through the ATCC).	disorders (e.g., hypertension,
	Exemplary mouse adipocyte	congestive heart failure, blood
	cells that may be used	vessel blockage, heart disease,
 	according to these assays	stroke, impotence and/or as
 	 include 3T3-L1 cells. 3T3-L1	described below under
 	is an adherent mouse	"Immune Activity",
	 preadipocyte cell line that is a	"Cardiovascular Disorders",
	continuous substrain of 3T3	and/or "Blood-Related

through clonal isolatio undergo a pre-adipocy adipose-like conversio appropriate differentia conditions known in th			fibroblast cells developed	Disorders"), immune disorders
undergo a pre-adipocy adipose-like conversio appropriate differential conditions known in the			through clonal isolation and	(e.g., as described below under
adipose-like conversio appropriate differential conditions known in the conditions known in the conditions con			undergo a pre-adipocyte to	"Immune Activity"), neural
appropriate differential conditions known in the conditions known in the conditions has a condition to the conditions conditions conditions has a condition to the conditions conditions has a condition to the conditions c			adipose-like conversion under	disorders (e.g., as described
conditions known in th	-		appropriate differentiation	below under "Neural Activity
			conditions known in the art.	and Neurological Diseases"),
				and infection (e.g., as
		-1		described below under
	-			"Infectious Disease").
				A highly preferred indication
				is diabetes mellitus. An
				additional highly preferred
				indication is a complication
				associated with diabetes (e.g.,
				diabetic retinopathy, diabetic
				nephropathy, kidney disease
				(e.g., renal failure,
				nephropathy and/or other
				diseases and disorders as
		•		described in the "Renal
				Disorders" section below),
				diabetic neuropathy, nerve
				disease and nerve damage
				(e.g., due to diabetic
				neuropathy), blood vessel
				blockage, heart disease, stroke,
				impotence (e.g., due to diabetic
				neuropathy or blood vessel
				blockage), seizures, mental
				confusion, drowsiness,
				nonketotic hyperglycemic-

hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as	described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below),	(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the	urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.

Additional highly preferred indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	Iymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,	prostate, lung, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer.	Highly preferred indications	include lipomas and	liposarcomas. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,
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	^	1190	Activation of	Assays for the activation of	A preferred embodiment of	
<u> </u>			transcription	transcription through the	the invention includes a	
			through serum	Serum Response Element	method for inhibiting (e.g.,	
			response element in	(SRE) are well-known in the	reducing) TNF alpha	
			immune cells (such	art and may be used or	production. An alternative	
		200	as T-cells).	routinely modified to assess	preferred embodiment of the	
			`	the ability of polypeptides of	invention includes a method	
				the invention (including	for stimulating (e.g.,	
				antibodies and agonists or	increasing) TNF alpha	
				antagonists of the invention) to	production. Preferred	
				regulate the serum response	indications include blood	
<u></u>				factors and modulate the	disorders (e.g., as described	
·				expression of genes involved	below under "Immune	
4. • •		-8.7		in growth. Exemplary assays	Activity", "Blood-Related	
				for transcription through the	Disorders", and/or	
				SRE that may be used or	"Cardiovascular Disorders"),	
				routinely modified to test SRE	Highly preferred indications	
				activity of the polypeptides of	include autoimmune diseases	
		-11-12		the invention (including	(e.g., rheumatoid arthritis,	
				antibodies and agonists or	systemic lupus erythematosis,	
				antagonists of the invention)	Crohn"s disease, multiple	
				include assays disclosed in	sclerosis and/or as described	
				Berger et al., Gene 66:1-10	below), immunodeficiencies	
				(1998); Cullen and Malm,	(e.g., as described below),	
				Methods in Enzymol 216:362-	boosting a T cell-mediated	
				368 (1992); Henthorn et al.,	immune response, and	
-				Proc Natl Acad Sci USA	suppressing a T cell-mediated	
				85:6342-6346 (1988); and	immune response. Additional	
				Black et al., Virus Genes	highly preferred indications	
				12(2):105-117 (1997), the	include inflammation and	_

inflammatory disorders, and treating joint damage in patients with rheumatoid	arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases	(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and	cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast,	lung, colon, pancreauc, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute
content of each of which are herein incorporated by reference in its entirety. T	cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic	activity.		

	ЯНСОВІК	100	Activation of	A seave for the activation of	lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
242	HHGDF16	1190	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under

	transcription through the AP1	"Infectious Disease"). Highly
	response element that may be	preferred indications include
	used or routinely modified to	autoimmune diseases (e.g.,
	test AP1-response element	rheumatoid arthritis, systemic
-	activity of polypeptides of the	lupus erythematosis, multiple
	invention (including antibodies	sclerosis and/or as described
	and agonists or antagonists of	below) and
	the invention) include assays	immunodeficiencies (e.g., as
	disclosed in Berger et al., Gene	described below). Additional
	66:1-10 (1988); Cullen and	highly preferred indications
	Malm, Methods in Enzymol	include inflammation and
	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	272(49):30806-30811 (1997);	lymphoma, and/or as described
	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,
	reference in its entirety.	lung, colon, pancreatic,
	Human T cells that may be	esophageal, stomach, brain,
	used according to these assays	liver, and urinary cancer. Other
	are publicly available (e.g.,	preferred indications include
	through the ATCC).	benign dysproliferative
	Exemplary human T cells that	disorders and pre-neoplastic
	may be used according to these	conditions, such as, for
	assays include the SUPT cell	example, hyperplasia,
	line, which is an IL-2 and IL-4	metaplasia, and/or dysplasia.

on-culture arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	ation of he AP1 include neoplastic diseases e well- d may be "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related ate growth Disorders"), and infection (e.g., an infectious disease as described below under the AP1 "Infectious Disease"). Highly at may be preferred indications include autoimmune diseases (e.g., antoimmune disease
responsive suspension-culture cell line.	Assays for the activation of transcription through the AP1 response element are well-tin known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the inventions). Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to
	Activation of transcription through AP1 response element in immune cells (such as T-cells).
	1191
	HHGDW43
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	activity of polypeptides of the	lupus erythematosis, multiple
	invention (including antibodies	sclerosis and/or as described
	and agonists or antagonists of	below) and
	the invention) include assays	immunodeficiencies (e.g., as
	 disclosed in Berger et al., Gene	described below). Additional
	66:1-10 (1988); Cullen and	highly preferred indications
	Malm, Methods in Enzymol	include inflammation and
	 216:362-368 (1992); Henthorn	inflammatory disorders.
	 et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	272(49):30806-30811 (1997);	lymphoma, and/or as described
•	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	 contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,
	 reference in its entirety.	lung, colon, pancreatic,
	 Human T cells that may be	esophageal, stomach, brain,
	used according to these assays	liver, and urinary cancer. Other
	 are publicly available (e.g.,	preferred indications include
	 through the ATCC).	benign dysproliferative
	Exemplary human T cells that	disorders and pre-neoplastic
	 may be used according to these	conditions, such as, for
	assays include the SUPT cell	example, hyperplasia,
	line, which is an IL-2 and IL-4	metaplasia, and/or dysplasia.
	responsive suspension-culture	Preferred indications include
	cell line.	arthritis, asthma, AIDS,
		allergy, anemia, pancytopenia,
	.,	leukopenia, thrombocytopenia,

Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of imnune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	Highly preferred indications include allergy and asthma. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune
	Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) to modulate IL-10 production and/or T-cell proliferation include, for
	Production of IL-10 and activation of T-cells.
	1191
	HHGDW43
	243

disclosed and/or cited in: Robinson, DS, et al., "Th-2 cytokines in allergic disease" Br Med Bull; 56 (4): 956-968 (2000), and Cohn, et al., "T- helper type 2 cell-directed therapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral

				from cord blood.	
	HHPDX20	1192	Activation of	Assays for the activation of	A highly preferred indication
244	~		transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
			response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
				functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
				may be used to identify factors	described in the "Renal
				that activate the cAMP	Disorders" section below),
				signaling pathway. CREB	diabetic neuropathy, nerve
				plays a major role in	disease and nerve damage
				adipogenesis, and is involved	(e.g., due to diabetic
				in differentiation into	neuropathy), blood vessel
				adipocytes. CRE contains the	blockage, heart disease, stroke,
			-	binding sequence for the	impotence (e.g., due to diabetic
				transcription factor CREB	neuropathy or blood vessel
				(CRE binding protein).	blockage), seizures, mental
				Exemplary assays for	confusion, drowsiness,
				transcription through the	nonketotic hyperglycemic-
				cAMP response element that	hyperosmolar coma,
				may be used or routinely	cardiovascular disease (e.g.,

modified to test cAMP-	heart disease, atherosclerosis,
response element activity of	microvascular disease,
polypeptides of the invention	hypertension, stroke, and other
(including antibodies and	diseases and disorders as
agonists or antagonists of the	described in the
invention) include assays	"Cardiovascular Disorders"
disclosed in Berger et al., Gene	section below), dyslipidemia,
66:1-10 (1998); Cullen and	endocrine disorders (as
Malm, Methods in Enzymol	described in the "Endocrine
216:362-368 (1992); Henthorn	Disorders" section below),
et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
et al., Mol Cell Biol	blindness), ulcers and impaired
20(3):1008-1020 (2000); and	wound healing, and infection
Klemm et al., J Biol Chem	(e.g., infectious diseases and
273:917-923 (1998), the	disorders as described in the
contents of each of which are	"Infectious Diseases" section
herein incorporated by	below, especially of the
reference in its entirety. Pre-	urinary tract and skin), carpal
adipocytes that may be used	tunnel syndrome and
according to these assays are	Dupuytren's contracture).
publicly available (e.g.,	Additional highly preferred
through the ATCC) and/or	indications are complications
may be routinely generated.	associated with insulin
Exemplary mouse adipocyte	resistance.
cells that may be used	
according to these assays	-
include 3T3-L1 cells. 3T3-L1	
is an adherent mouse	
preadipocyte cell line that is a	
continuous substrain of 3T3	

<u>H</u>	HHPDX20	1192	Endothelial Cell Apoptosis	fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumor is associated with tumor blood supply. Exemplary associated to test capase apoptosis that may be used or routinely modified to test capase apoptosis activity of	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation.
				polypeptides of the invention (including antibodies and	stimulating apoptosis of endothelial cells. An
				agonists or antagonists of the invention) include the assays disclosed in Lee et al., FEBS	alternative highly preferred embodiment of the invention includes a method for

		Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)
		Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.
		209-218 (2000); and Karsan	A highly preferred
		and Harlan, J Atheroscler	embodiment of the invention
		Thromb 3(2): 75-80 (1996);	includes a method for
		the contents of each of which	stimulating angiogenisis. An
	-	are herein incorporated by	alternative highly preferred
		reference in its entirety.	embodiment of the invention
·		Endothelial cells that may be	includes a method for
-		used according to these assays	inhibiting angiogenesis. A
		are publicly available (e.g.,	highly preferred embodiment
		through commercial sources).	of the invention includes a
		Exemplary endothelial cells	method for reducing cardiac
	 	that may be used according to	hypertrophy. An alternative
	 	these assays include bovine	highly preferred embodiment
		aortic endothelial cells	of the invention includes a
		(bAEC), which are an example	method for inducing cardiac
	 	of endothelial cells which line	hypertrophy. Highly
		blood vessels and are involved	preferred indications include
		in functions that include, but	neoplastic diseases (e.g., as
		are not limited to,	described below under
		angiogenesis, vascular	"Hyperproliferative
		permeability, vascular tone,	Disorders"), and disorders of
		and immune cell extravasation.	the cardiovascular system
			(e.g., heart disease, congestive
•			heart failure, hypertension,
			aortic stenosis,
			cardiomyopathy, valvular
			regurgitation, left ventricular
			dysfunction, atherosclerosis
			and atherosclerotic vascular

disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,
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y and	imors,	ry		na,		ž,		lymphangiosarcoma. Highly	also	as,	colon,	ıl,	and .	red	mign	dysproliferative disorders and	pre-neoplastic conditions, such	rplasia,	splasia.	cations	isease,	is,	hypertension, coronary artery	_	s,,	s	sms,	þ	uch as	
hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary		hemangioendothelioma,		haemangiopericytoma,	ę,	rcoma.	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	ve disor	conditi	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	corona	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud's	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	itis,
gioma (ous), gl	ectasia,	angiomatosis,	gioendo	angiosarcoma,	ngioper	lymphangioma,	angiosa	ed indic	e cancer	e, breas	atic, esc	th, brai	zancer	ions inc	liferativ	oplastic	exampl	asia, an	preferi	clude an	s, ather	ension,	e, inflan	itides, F	and Re	nenom,	sis; ver	atic disc	thrombophlebitis,
heman	cavern	telangi	angion	heman	angios	haema	lympha	lympha	preferr	include	prostat	pancre	stomac	urinary	indicat	dyspro	pre-ne	as, for	metapl	Highly	also in	such a	hypert	disease	vascul	disease	phenor	restenc	lymph	throm
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		lymphangitis, and
 		lymphedema; and other
		vascular disorders such as
		peripheral vascular disease,
 		and cancer. Highly
 		preferred indications also
 		include trauma such as
 		wounds, burns, and injured
 		tissue (e.g., vascular injury
 		such as, injury resulting from
 		balloon angioplasty, and
 		atheroschlerotic lesions),
		implant fixation, scarring,
		ischemia reperfusion injury,
 		rheumatoid arthritis,
		cerebrovascular disease, renal
 		diseases such as acute renal
		failure, and osteoporosis.
 -		Additional highly preferred
 		indications include stroke,
 		graft rejection, diabetic or
 		other retinopathies, thrombotic
 -		and coagulative disorders,
 		vascularitis, lymph
		angiogenesis, sexual disorders,
		age-related macular
 -		degeneration, and treatment
		/prevention of endometriosis
 	-	and related conditions.
 		Additional highly preferred
		indications include fibromas.

					heart disease, cardiac arrest,
					vascular disease.
					Preferred indications include
					blood disorders (e.g., as
					described below under
					"Immune Activity", "Blood-
					Kelated Disorders, and/or "Cardiovascular Disorders")
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
		·			described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
		·			inflammatory bowel disease
					and Crohn's disease), and pain
					management.
244	HHPDX20	1192	IL-10 in Human T-cell 293T		
	HHPGO40	1193	Proliferation of	Assays for the regulation (i.e.	Highly preferred indications
245			immune cells (such	increases or decreases) of	include asthma, allergy,
			as the HMC-1	viability and proliferation of	mastocytosis (a rare,
			human mast cell	cells in vitro are well-known in	heterogeneous disorder

the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of eosinophil cells and cell lines. For example, the CellTiter-Gloō Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the presence of meatabolically active cells. Mast cells are found in connective and mucosal tissues throughout the body. Mast cell activation (via immunoglobulin E-antigen, promoted by T helper cell type 2 cytokines) is an important component of allergic disease. Dysregulation of mast cell integration survival. Mast cell integrations varvival. Mast cell integration survival. Mast cell integration survival. Mast cell integration or survival. Mast cell integration survival.	characterized by excessive	accumulation of mast cells,	and their proliferation and	action in the skin, central	nervous system, and other		also include hematopoietic and	ls immunological disorders (e.g.,	as described below under	''Immune Activity", and	"Blood-Related Disorders"),	infection (e.g., as described	below under "Infectious	f Disease"), autoimmune		arthritis, systemic lupus	erythematosis, multiple	sclerosis and/or as described	below), and	immunodeficiencies (e.g., as	e described below).	ia		ψ.						So	
	the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate viability and	proliferation of eosinophil cells	and cell lines. For example,	the CellTiter-Gloô	Luminescent Cell Viability	Assay (Promega Corp.,	Madison, WI, USA) can be	used to measure the number o	viable cells in culture based on	quantitation of the ATP	present which signals the	presence of metabolically	active cells. Mast cells are	found in connective and	mucosal tissues throughout the	body. Mast cell activation (vi	immunoglobulin E -antigen,	promoted by T helper cell type	2 cytokines) is an important	component of allergic disease.	Dysregulation of mast cell	apoptosis may play a role in	allergic disease and mast cell	tumor survival. Mast cell lines	that may be used according to
	line)								_										-												
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these assays are publicly available and/or may be routinely generated. Exemplary mast cells that may be used according to these assays include HMC-1, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.		Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be
	Glucose Production in H4IIE	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1193	1193
	HHPGO40	HHPGO40
	245	245

	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.
used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for
	Caspase (+paclitaxel) in SW480 Regulation of apoptosis of immune cells (such as mast cells).
	1194
,	HHPGO40
1500	246

example, in mast cells). Mast cells are found in connective	and mucosal tissues throughout the body, and their activation	via immunoglobulin E -	antigen, promoted by T helper	cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000); Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	3(2): 75-80 (1996); the
																									-			

of which are tted by antirety. at may be used se assays are le (e.g., roial sources). une cells that cording to these nast cells such nan mast cell		ctivation of A preferred embodiment of the invention includes a method for inhibiting (e.g., known in the production. An alternative juppeptides of invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune mplary assays https://doi.org/10.1001/2	ied to test SRE Highly preferred indications
contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	IL-2 in Human T- cell 2B9	Activation of Assays for the activation of transcription through serum response element in immune cells (such art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or	routinely modified to test SRE
	1194	1195	
	HHPT165	HHSDX28	
·	246	247	

include autoimmune diseases (e σ rheumatoid arthritis	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,
activity of the polypeptides of include the invention (including	or	antagonists of the invention) Crohi	include assays disclosed in sclerc	Berger et al., Gene 66:1-10 below	(1998); Cullen and Malm, (e.g.,	Methods in Enzymol 216:362- boost	368 (1992); Henthorn et al., immu		85:6342-6346 (1988); and immu		12(2):105-117 (1997), the include	content of each of which are inflan		reference in its entirety. T patier	cells that may be used arthri	s are	publicly available (e.g., Highl		Exemplary mouse T cells that (e.g.,	may be used according to these and/o	LL cell	line, which is an IL-2 Disor	Iture	of T cells with cytotoxic inclu		leuke	mela	malig	timo
activity of the inven	antibodie	antagoni	include a	Berger el	(1998); (Methods	368 (199	Proc Nat	85:6342-	Black et	12(2):10	content	herein in	reference	cells that	according	publicly	through t	Exempla	may be u	assays in	line, whi	depender	of T cells	activity.			•	
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lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication	is infection (e.g., an infectious	disease as described below
		-										_																		
	-																													
				-											-															

					under "Infectious Disease").
	HHSDX28	1195	Production of TNF	TNFa FMAT. Assays for	A highly preferred
247			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
***				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred
				wide variety of inflammatory	embodiment of the invention
				and cytotoxic effects on a	includes a method for
				variety of cells are well known	stimulating (e.g., increasing)
				in the art and may be used or	TNF alpha production.
				routinely modified to assess	Highly preferred indications
_				the ability of polypeptides of	include blood disorders (e.g.,
				the invention (including	as described below under
				antibodies and agonists or	"Immune Activity", "Blood-
				antagonists of the invention) to	Related Disorders", and/or
				mediate immunomodulation,	"Cardiovascular Disorders"),
				modulate inflammation and	Highly preferred indications
				cytotoxicity. Exemplary	include autoimmune diseases
				assays that test for	(e.g., rheumatoid arthritis,
				immunomodulatory proteins	systemic lupus erythematosis,
				evaluate the production of	Crohn"s disease, multiple
				cytokines such as tumor	sclerosis and/or as described
				necrosis factor alpha (TNFa),	below), immunodeficiencies
				and the induction or inhibition	(e.g., as described below),
				of an inflammatory or	boosting a T cell-mediated
				cytotoxic response. Such	immune response, and
				assays that may be used or	suppressing a T cell-mediated
			-	routinely modified to test	immune response. Additional
				immunomodulatory activity of	highly preferred indications
				polypeptides of the invention	include inflammation and

inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),
fincluding antibodies and in	the		disclosed in Miraglia et al., J ar	3-			091	_	Immunol 28(11):3886-3890 ur	(1198); Dahlen et al., J D	3593	ſ		(1997); and Nardelli et al., J ly		(1999), the contents of each of \mid tu	which are herein incorporated lu	by reference in its entirety.	Human dendritic cells that may liv	be used according to these pi	assays may be isolated using be	-	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in m		when activated by antigen	pu	upregulate T cell proliferation H	and functional activities.
	ag	i	ip	B	20	I			<u>. </u>	(1)	<u>, </u>	(1	· <u>11</u>			<u></u>	*	9	<u> </u>			te	0	<u> </u>		18		<u> </u>	n	
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plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	This reporter assay measures activation of the GATA-3 include allergy, asthma, and signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the production of transcription activation of transcription art and may be used or activation of the GATA3 response element are well-known in the art and may be used or activation of the GATA3 response element are well-known in the art and may be used or activation of the GATA3 response element are well-known in the art and may be used or activation of the GATA3 response element are well-known in the art and may be used or activation of the GATA3 response include blood disorders (e.g., an inflammatory disease as described below under activation of transcription art and may be used or activation of the GATA3 response include blood disorders (e.g., an inflammation and inflammation and inflammation and inflammatory disorders (e.g., an inflammation and inflammation and inflammation and inflammatory disorders.
-	Activation of Th transcription act through GATA-3 sig response element in hun immune cells (such as mast cells).
	1195
	HHSDX28
	247

	the ability of polynentides of	Related Disorders", and/or
	the invention (including	"Cardiovascular Disorders").
	antibodies and agonists or	Preferred indications include
	antagonists of the invention) to	autoimmune diseases (e.g.,
	regulate GATA3 transcription	rheumatoid arthritis, systemic
	factors and modulate	lupus erythematosis, multiple
	expression of mast cell genes	sclerosis and/or as described
	important for immune response	below) and
	development. Exemplary	immunodeficiencies (e.g., as
	assays for transcription	described below). Preferred
	through the GATA3 response	indications include neoplastic
	element that may be used or	diseases (e.g., leukemia,
	routinely modified to test	lymphoma, melanoma,
	GATA3-response element	prostate, breast, lung, colon,
	activity of polypeptides of the	pancreatic, esophageal,
	invention (including antibodies	stomach, brain, liver, and
	and agonists or antagonists of	urinary tract cancers and/or as
	the invention) include assays	described below under
	disclosed in Berger et al., Gene	"Hyperproliferative
	66:1-10 (1998); Cullen and	Disorders"). Other preferred
-	Malm, Methods in Enzymol	indications include benign
	216:362-368 (1992); Henthorn	dysproliferative disorders and
	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
	Quant Biol 64:563-571 (1999);	Preferred indications include
	Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
	J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
	Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
	Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,

multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.				A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method
14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.				Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess
	IgG in Human B cells	MCP-1 in HUVEC	TNFa in Human T-cell 293T	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
	1195	1195	1196	1196
	HHSDX28	HHSDX28	HILCF66	HILCF66
	247	247	248	248

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for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for	stimulating endothelial cell proliferation. An alternative highly preferred embodiment	of the invention includes a method for inhibiting	endothelial cell proliferation. A highly preferred	embodiment of the invention includes a method for	stimulating apoptosis of	alternative highly preferred	embodiment of the invention	includes a method for	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing) endothelial cell activation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing) the	activation of and/or	inactivating endothelial cells.
the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to	promote or inhibit cell proliferation, activation, and	for JNK and p38 kinase activity that may be used or	routinely modified to test JNK and p38 kinase-induced	activity of polypeptides of the invention (including antibodies	and agonists or antagonists of	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,
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A highly preferred embodiment of the invention includes a method for	stimulating angiogenisis. An alternative highly preferred	embodiment of the invention includes a method for	inhibiting angiogenesis. A highly preferred embodiment	of the invention includes a	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac
through the ATCC). Exemplary endothelial cells that may be used according to	these assays include human umbilical vein endothelial cells	(HUVEC), which are endothelial cells which line	venous blood vessels, and are involved in functions that	include, but are not limited to,	permeability, vascular tone,	and immune cell extravasation.							-										
					-																		

	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,
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-																		-												· ·	

telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other
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vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and
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vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammatory disorders (such as acute and chronic inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.		
		Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess
	MIP-1a in HMC	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1197	1197
	HJACG02	HJACG02
	249	249

activation or inhibition of the	NFkB signaling pathway in	Ku812 human basophil cell	line. Assays for the activation	or inhibition of transcription	through the NFKB response	element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate NFKB transcription	factors and modulate	expression of	immunomodulatory genes.	NFkB is important in the	pathogenesis of asthma.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and
inhibition of	transcription	through NFKB	response element in	immune cells (such	as basophils).				-																					
249																														

Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al. Proc Natl Acad Sci 11SA	85:6342-6346 (1988); Marone et al, Int Arch Allergy	Immunol 114(3):207-17 (1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Cells were pretreated with SID	supernatants or controls for 15-	of TNF was added to stimulate	the NFkB reporter. SEAP	activity was measured after 48	hours. Basophils that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary human basophil	cell lines that may be used	according to these assays	include Ku812, originally	established from a patient with	chronic myelogenous	leukemia. It is an immature	prebasophilic cell line that can	be induced to differentiate into	mature basophils. See, Kishi et	al., Leuk Res. 9:381-390	(1985); Blom et al., Eur J
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				11111111111111. 44.4047-74 (1774)	
				where the contents of each are	
				herein incorporated by	
				reference in its entirety.	
	HJACG30	1198	Activation of	Assays for the activation of	A preferred embodiment of
250			transcription	transcription through the	the invention includes a
,			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
			`	the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
		<u>.</u>		regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
,				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
		****		include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),
				Methods in Enzymol 216:362-	boosting a T cell-mediated
-10				368 (1992); Henthorn et al.,	immune response, and
				Proc Natl Acad Sci USA	suppressing a T cell-mediated

			85:6342-6346 (1988); and	immune response. Additional
			Black et al., virus Genes 12(2):105-117 (1997), the	nigniy preferred indications include inflammation and
			content of each of which are	inflammatory disorders, and
			herein incorporated by	treating joint damage in
			reference in its entirety. T	patients with rheumatoid
			cells that may be used	arthritis. An additional highly
			according to these assays are	preferred indication is sepsis.
			publicly available (e.g.,	Highly preferred indications
			through the ATCC).	include neoplastic diseases
			Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
			may be used according to these	and/or as described below
			assays include the CTLL cell	under "Hyperproliferative
			line, which is an IL-2	Disorders"). Additionally,
- 14			dependent suspension culture	highly preferred indications
			of T cells with cytotoxic	include neoplasms and
			activity.	cancers, such as, for example,
		•		leukemia, lymphoma,
				melanoma, glioma (e.g.,
				malignant glioma), solid
	-			tumors, and prostate, breast,
				lung, colon, pancreatic,
				esophageal, stomach, brain,
				liver and urinary cancer. Other
-				preferred indications include
				benign dysproliferative
				disorders and pre-neoplastic
				conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
				Preferred indications include

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HJACG30

its lits	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease to (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel
incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes
	Stimulation of insulin secretion from pancreatic beta cells.
	1198
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blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma,	cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease,	hypertension, stroke, and other diseases and disorders as described in the	"Cardiovascular Disorders" section below), dyslipidemia,	described in the "Endocrine Disorders" section below).	neuropathy, vision impairment (e.g., diabetic retinopathy and	blindness), ulcers and impaired wound healing, and infection	(e.g., infectious diseases and disorders as described in the	"Infectious Diseases" section below, especially of the	urinary tract and skin), carpal tunnel syndrome and	Dupuytren's contracture). An additional highly preferred	indication is obesity and/or	obesity. Additional highly	preferred indications include
Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic	cells) by polypeptides of the invention (including antibodies and agonists or antagonists of	the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt	2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Vim	K.H., et al., FEBS Lett, 377(2):237-9 (1995); and,	Miraglia S et. al., Journal of Biomolecular Screening,	4:193-204 (1999), the contents of each of which is herein	incorporated by reference in its entirety. Pancreatic cells that	may be used according to these assays are publicly available	(e.g., through the ATCC) and/or may be routinely	generated. Exemplary pancreatic cells that may be	used according to these assays include rat INS-1 cells INS-1	cells are a semi-adherent cell	line established from cells

we we high	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkins lymphoma, non-Hodgkins lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for
isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the
•	Activation of transcription through GAS response element in immune cells (such as T-cells).
(1199
	HJBCU04
	251

	and agonists or antagonists of	metaplasia, and/or dysplasia.
	the invention) include assays	Preferred indications include
	disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
	66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
1	Malm, Methods in Enzymol	lupus erythematosis, multiple
	216:362-368 (1992); Henthorn	sclerosis and/or as described
	et al., Proc Natl Acad Sci USA	below), immunodeficiencies
	85:6342-6346 (1988);	(e.g., as described below),
	Matikainen et al., Blood	boosting a T cell-mediated
	93(6):1980-1991 (1999); and	immune response, and
	Henttinen et al., J Immunol	suppressing a T cell-mediated
	155(10):4582-4587 (1995), the	immune response. Additional
	contents of each of which are	preferred indications include
	herein incorporated by	inflammation and
	reference in its entirety.	inflammatory disorders.
	Exemplary mouse T cells that	Highly preferred indications
	may be used according to these	include blood disorders (e.g.,
	assays are publicly available	as described below under
della	(e.g., through the ATCC).	"Immune Activity", "Blood-
	Exemplary T cells that may be	Related Disorders", and/or
	used according to these assays	"Cardiovascular Disorders"),
	include the CTLL cell line,	and infection (e.g., viral
	which is a suspension culture	infections, tuberculosis,
	of IL-2 dependent cytotoxic T	infections associated with
	cells.	chronic granulomatosus
		disease and malignant
		osteoporosis, and/or an
		infectious disease as described
		below under "Infectious
		Disease"). An additional
		preferred indication is

					idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia.
					acute lymphocytic anemia (ALL), plasmacytomas,
					multiple myeloma, arthritis, AIDS, granulomatous disease,
100.0					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis, suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
<u></u>					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
751	HJBCU04	1199	Production of IL-4	IL-4 FMAT. Assays for	A highly preferred
167				immunomodulatory proteins	embodiment of the invention
				secreted by TH2 cells that	includes a method for
				stimulate B cells, T cells,	stimulating (e.g., increasing)
				macrophages and mast cells	IL-4 production. An alternative
				and promote polarization of	highly preferred embodiment
				CD4+ cells into TH2 cells are	of the invention includes a
				well known in the art and may	method for inhibiting (e.g.,
		11-1-		be used or routinely modified	reducing) IL-4 production.
				to assess the ability of	A highly preferred indication
				polypeptides of the invention	includes asthma. A highly
				(including antibodies and	preferred indication includes
				agonists or antagonists of the	allergy. A highly preferred

	invention) to mediate	indication includes rhinitis.
	immunomodulation, stimulate	Additional highly preferred
	immune cells, modulate	indications include
	immune cell polarization,	inflammation and
	and/or mediate humoral or	inflammatory disorders.
	cell-mediated immunity.	Highly preferred indications
	Exemplary assays that test for	include neoplastic diseases
-	immunomodulatory proteins	(e.g., leukemia, lymphoma,
	evaluate the production of	melanoma, and/or as described
	cytokines, such as IL-4, and	below under
	the stimulation of immune	"Hyperproliferative
	cells, such as B cells, T cells,	Disorders"). Preferred
	macrophages and mast cells.	indications include neoplasms
	Such assays that may be used	and cancers, such as, for
	or routinely modified to test	example, leukemia, lymphoma,
	immunomodulatory activity of	melanoma, and prostate,
	polypeptides of the invention	breast, lung, colon, pancreatic,
	(including antibodies and	esophageal, stomach, brain,
100	agonists or antagonists of the	liver and urinary cancer. Other
-	invention) include the assays	preferred indications include
	disclosed in Miraglia et al., J	benign dysproliferative
	Biomolecular Screening 4:193-	disorders and pre-neoplastic
	204 (1999); Rowland et al.,	conditions, such as, for
	"Lymphocytes: a practical	example, hyperplasia,
	approach" Chapter 6:138-160	metaplasia, and/or dysplasia.
	(2000); Gonzalez et al., J Clin	Preferred indications include
	Lab Anal 8(5):277-283 (1194);	blood disorders (e.g., as
	Yssel et al., Res Immunol	described below under
	144(8):610-616 (1993); Bagley	"Immune Activity", "Blood-
	et al., Nat Immunol 1(3):257-	Related Disorders", and/or
	261 (2000); and van der Graaff	"Cardiovascular Disorders").

				et al Rheumatology (Oxford)	Preferred indications include
-				38/3):714-220 (1000) the	autoimmuna disasses (a g
				30(3):21+-220 (1333), uic	autominimic discases (e.g.,
				contents of each of which are	rneumatoid arthritis, systemic
				herein incorporated by	lupus erythematosis, multiple
				reference in its entirety.	sclerosis and/or as described
				Human T cells that may be	below) and
-				used according to these assays	immunodeficiencies (e.g., as
				may be isolated using	described below). Preferred
				techniques disclosed herein or	indications include anemia,
				otherwise known in the art.	pancytopenia, leukopenia,
				Human T cells are primary	thrombocytopenia, Hodgkin's
				human lymphocytes that	disease, acute lymphocytic
				mature in the thymus and	anemia (ALL),
				express a T cell receptor and	plasmacytomas, multiple
				CD3, CD4, or CD8. These	myeloma, Burkitt's lymphoma,
				cells mediate humoral or cell-	arthritis, AIDS, granulomatous
				mediated immunity and may	disease, inflammatory bowel
•				be preactivated to enhance	disease, sepsis, neutropenia,
				responsiveness to	neutrophilia, psoriasis,
	_			immunomodulatory factors.	suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
	•				indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
HJBCU04	-	199	SEAP in SW480		

251					
252	HJBCY35	1200	SEAP in 3T3L1		
030	HJBCY35	1200	Regulation of	Assays for the regulation of	A highly preferred indication
767			viability and	viability and proliferation of	is diabetes mellitus. An
	-		proliferation of	cells in vitro are well-known in	additional highly preferred
			pancreatic beta	the art and may be used or	indication is a complication
			cells.	routinely modified to assess	associated with diabetes (e.g.,
				the ability of polypeptides of	diabetic retinopathy, diabetic
				the invention (including	nephropathy, kidney disease
				antibodies and agonists or	(e.g., renal failure,
				antagonists of the invention) to	nephropathy and/or other
				regulate viability and	diseases and disorders as
				proliferation of pancreatic beta	described in the "Renal
				cells. For example, the Cell	Disorders" section below),
				Titer-Glo luminescent cell	diabetic neuropathy, nerve
				viability assay measures the	disease and nerve damage
				number of viable cells in	(e.g., due to diabetic
				culture based on quantitation	neuropathy), blood vessel
		··-		of the ATP present which	blockage, heart disease, stroke,
				signals the presence of	impotence (e.g., due to diabetic
				metabolically active cells.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
				test regulation of viability and	nonketotic hyperglycemic-
				proliferation of pancreatic beta	hyperosmolar coma,
				cells by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
				the invention) include assays	hypertension, stroke, and other
				disclosed in: Friedrichsen BN,	diseases and disorders as

				et al Mol Endocrinol	described in the
				15(1):136-48 (2001); Huotari	"Cardiovascular Disorders"
				MA, et al., Endocrinology,	section below), dyslipidemia,
				139(4):1494-9 (1998); Hugl	endocrine disorders (as
				SR, et al., J Biol Chem 1998	described in the "Endocrine
				Jul 10;273(28):17771-9	Disorders" section below),
				(1998), the contents of each of	neuropathy, vision impairment
				which is herein incorporated	(e.g., diabetic retinopathy and
				by reference in its entirety.	blindness), ulcers and impaired
				Pancreatic cells that may be	wound healing, and infection
				used according to these assays	(e.g., infectious diseases and
				are publicly available (e.g.,	disorders as described in the
				through the ATCC) and/or	"Infectious Diseases" section
				may be routinely generated.	below, especially of the
				Exemplary pancreatic cells that	urinary tract and skin), carpal
				may be used according to these	tunnel syndrome and
				assays include rat INS-1 cells.	Dupuytren's contracture). An
				INS-1 cells are a semi-	additional highly preferred
				adherent cell line established	indication is obesity and/or
				from cells isolated from an X-	complications associated with
				ray induced rat transplantable	obesity. Additional highly
				insulinoma. These cells retain	preferred indications include
				characteristics typical of native	weight loss or alternatively,
				pancreatic beta cells including	weight gain. Additional highly
				glucose inducible insulin	preferred indications are
				secretion. References: Asfari	complications associated with
				et al. Endocrinology 1992	insulin resistance.
				130:167.	
	HJBCY35	1200	Activation of	Kinase assay. Kinase assays,	A highly preferred
252			Skeletal Mucle Cell	for example an GSK-3 kinase	embodiment of the invention
			PI3 Kinase	assay, for PI3 kinase signal	includes a method for

survivial are well-know art and may be used or routinely modified to as the ability of polypeptid the invention (including antibodies and agonists antagonists of the inven promote or inhibit glucc metabolism and cell sur Exemplary assays for Pl kinase activity that may used or routinely modific test P13 kinase-induced of polypeptides of the invention (including ant and agonists or antagon the invention) include a disclosed in Forrer et al Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of which are herein incorp by reference in its entire Rat myoblast cells that:	glucose metabolism and cell	II An alternative highly preferred
art and may be used or routinely modified to as the ability of polypeptid the invention (including antibodies and agonists antibodies and agonists antibodies and agonists of the inven promote or inhibit glucc metabolism and cell sur Exemplary assays for Pl kinase activity that may used or routinely modifit test Pl3 kinase-induced of polypeptides of the invention (including anti and agonists or antagon the invention) include a disclosed in Forrer et al Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of which are herein incorp by reference in its entire Rat myoblast cells that:	survivial are well-known in the	
routinely modified to as the ability of polypeptid the invention (including antibodies and agonists antagonists of the inven promote or inhibit gluco metabolism and cell sur Exemplary assays for Pl kinase activity that may used or routinely modifit test PI3 kinase-induced of polypeptides of the invention (including anta and agonists or antagon the invention) include a disclosed in Forrer et al Chem 379(8-9):1101-11 (1998); Nikoulina et al Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of which are herein incorp by reference in its entire Rat myoblast cells that:	art and may be used or	includes a method for
the ability of polypeptid the invention (including antibodies and agonists antagonists of the invention promote or inhibit glucc metabolism and cell sur Exemplary assays for Pl kinase activity that may used or routinely modifit test P13 kinase-induced of polypeptides of the invention (including ant and agonists or antagon the invention (including ant and agonists or antagon the invention) include a disclosed in Forrer et al Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of which are herein incorp by reference in its entire Rat myoblast cells that:	routinely modified to assess	s decreasing muscle cell
the invention (including antibodies and agonists antagonists of the inven promote or inhibit glucometabolism and cell sur Exemplary assays for Pl kinase activity that may used or routinely modifit test P13 kinase-induced of polypeptides of the invention (including ant and agonists or antagon the invention) include a disclosed in Forrer et al Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of which are herein incorp by reference in its entire Rat myoblast cells that:	the ability of polypeptides of	
antibodies and agonists antagonists of the inven promote or inhibit glucc metabolism and cell sur Exemplary assays for Pl kinase activity that may used or routinely modifit test Pl3 kinase-induced of polypeptides of the invention (including ant and agonists or antagon the invention) include a disclosed in Forrer et al Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of which are herein incorp by reference in its entire Rat myoblast cells that:	the invention (including	embodiment of the invention
antagonists of the inven promote or inhibit glucc metabolism and cell sur Exemplary assays for Pl kinase activity that may used or routinely modifit test P13 kinase-induced of polypeptides of the invention (including ant and agonists or antagon the invention) include a disclosed in Forrer et al Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of e which are herein incorp by reference in its entire Rat myoblast cells that:	antibodies and agonists or	includes a method for
promote or inhibit glucc metabolism and cell sur Exemplary assays for Pl kinase activity that may used or routinely modifit test P13 kinase-induced of polypeptides of the invention (including ant and agonists or antagon the invention) include a disclosed in Forrer et al Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of which are herein incorp by reference in its entire Rat myoblast cells that:	antagonists of the invention) to	1) to stimulating muscle cell
Exemplary assays for Pl kinase activity that may used or routinely modificatest P13 kinase-induced of polypeptides of the invention (including ant and agonists or antagon the invention) include and disclosed in Forrer et al Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of which are herein incorp by reference in its entire Rat myoblast cells that:	promote or inhibit glucose	proliferation. In a specific
Exemplary assays for Pl kinase activity that may used or routinely modifit test Pl3 kinase-induced of polypeptides of the invention (including ant and agonists or antagon) the invention) include a disclosed in Forrer et al. (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of e which are herein incorp by reference in its entire Rat myoblast cells that	metabolism and cell survival.	al. embodiment, skeletal muscle
kinase activity that may used or routinely modifit test P13 kinase-induced of polypeptides of the invention (including ant and agonists or antagon the invention) include a disclosed in Forrer et al. (Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of which are herein incorp by reference in its entire Rat myoblast cells that:	Exemplary assays for PI3	cell proliferation is stimulated.
used or routinely modifitest P13 kinase-induced of polypeptides of the invention (including ant and agonists or antagon the invention) include a disclosed in Forrer et al. Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of the which are herein incorp by reference in its entire Rat myoblast cells that:	kinase activity that may be	An alternative highly preferred
test PI3 kinase-induced of polypeptides of the invention (including ant and agonists or antagon the invention) include a disclosed in Forrer et al. Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of the which are herein incorp by reference in its entire Rat myoblast cells that:	used or routinely modified to	to embodiment of the invention
of polypeptides of the invention (including ant and agonists or antagon the invention) include a disclosed in Forrer et al. Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of et which are herein incorp by reference in its entire Rat myoblast cells that	test PI3 kinase-induced activity	vity includes a method for
invention (including ant and agonists or antagonithe invention) include a disclosed in Forrer et al. Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of experience in its entire by reference in its entire Rat myoblast cells that	of polypeptides of the	inhibiting muscle cell
and agonists or antagonithe invention) include as disclosed in Forrer et al. Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of which are herein incorpiby reference in its entire Rat myoblast cells that	invention (including antibodies	
the invention) include a disclosed in Forrer et al. Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of € which are herein incorp by reference in its entire Rat myoblast cells that	and agonists or antagonists of	of embodiment, skeletal muscle
disclosed in Forrer et al. Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of e which are herein incorp by reference in its entire Rat myoblast cells that	the invention) include assays	s cell proliferation is inhibited.
Chem 379(8-9):1101-11 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of et which are herein incorpuby reference in its entire Rat myoblast cells that	disclosed in Forrer et al., Biol	iol A preferred embodiment of
(1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of 6 which are herein incorp by reference in its entire Rat myoblast cells that	Chem 379(8-9):1101-1110	the invention includes a
Diabetes 49(2):263-271 (2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of e which are herein incorp by reference in its entire Rat myoblast cells that	(1998); Nikoulina et al.,	method for stimulating muscle
(2000); and Schreyer et Diabetes 48(8):1662-16 (1999), the contents of e which are herein incorp by reference in its entire Rat myoblast cells that	Diabetes 49(2):263-271	cell differentiation. In a
Diabetes 48(8):1662-16 (1999), the contents of e which are herein incorp by reference in its entire Rat myoblast cells that	(2000); and Schreyer et al.,	
(1999), the contents of e which are herein incorposition by reference in its entire Rat myoblast cells that	Diabetes 48(8):1662-1666	muscle cell differentiation is
which are herein incorpout to the senting that its entire. Rat myoblast cells that its entire.	(1999), the contents of each of	of stimulated. An alternative
by reference in its entire Rat myoblast cells that 1	which are herein incorporated	ed highly preferred embodiment
Rat myoblast cells that i	by reference in its entirety.	of the invention includes a
•	Rat myoblast cells that may be	
used according to these	used according to these assays	ays cell differentiation. In a
are publicly available (e	are publicly available (e.g.,	specific embodiment, skeletal

												<u> </u>		_																
muscle cell differentiation is	inhibited. Highly preferred	indications include disorders of	the musculoskeletal system.	Preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), endocrine	disorders (e.g., as described	below under "Endocrine	Disorders"), neural disorders	(e.g., as described below under	"Neural Activity and	Neurological Diseases"), blood	disorders (e.g., as described	below under "Immune	Activity", "Cardiovascular	Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity"), and infection (e.g.,	as described below under	winfectious Disease"). A	highly preferred indication is	diabetes mellitus.	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic
through the ATCC).	Exemplary rat myoblast cells	that may be used according to	these assays include L6 cells.	L6 is an adherent rat myoblast	cell line, isolated from primary	cultures of rat thigh muscle,	that fuses to form	multinucleated myotubes and	striated fibers after culture in	differentiation media.			-																	
			-			,		-				-																		
									-																					

	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g.,	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence	(e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired
	i											-					-														
-																									,					-	
																1-2-1		40 80													

wound healing, infections (e.g., infectious diseases and disorders as described in the	"Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuvtren's contracture).	An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively.	weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculockeletal system.	including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include: myopathy,	atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital

heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.		Assays for the activation of transcription through the Serum Response Element art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antagonists of the invention) to regulate serum response
	IL-2 in Human T-cell 293T	Activation of transcription through serum response element in immune cells (such as natural killer cells).
	1201	1201
	HJMBI18	HJMBI18
	253	253

below under "Immune Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and
expression of genes involved in growth and upregulate the	function of growth-related	genes in many cell types.	Exemplary assays for	transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,
						<u></u>			47-,				<u> </u>	_					· · · · · · · · · · · · · · · · · · ·			·, ·							

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cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast,	lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benign dysproliferative disorders and pre-neoplastic	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	anemia, pancytopenia, leukopenia, thrombocytopenia,	Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple	myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel	disease, neutropenia, neutrophilia, psoriasis, suppression of immune	reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,
which is a human natural killer cell line with cytolytic and cytotoxic activity.								
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					cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease")
254	HJMBM38	1202	Endothelial Cell Apoptosis	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention

	Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)
	Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.
	 209-218 (2000); and Karsan	A highly preferred
	and Harlan, J Atheroscler	embodiment of the invention
	 Thromb 3(2): 75-80 (1996);	includes a method for
	the contents of each of which	stimulating angiogenisis. An
	 are herein incorporated by	alternative highly preferred
	 reference in its entirety.	embodiment of the invention
	 Endothelial cells that may be	includes a method for
	used according to these assays	inhibiting angiogenesis. A
	 are publicly available (e.g.,	highly preferred embodiment
	through commercial sources).	of the invention includes a
	 Exemplary endothelial cells	method for reducing cardiac
	that may be used according to	hypertrophy. An alternative
	these assays include bovine	highly preferred embodiment
	aortic endothelial cells	of the invention includes a
	 (bAEC), which are an example	method for inducing cardiac
	of endothelial cells which line	hypertrophy. Highly
	blood vessels and are involved	preferred indications include
	 in functions that include, but	neoplastic diseases (e.g., as
	are not limited to,	described below under
	angiogenesis, vascular	"Hyperproliferative
	permeability, vascular tone,	Disorders"), and disorders of
	and immune cell extravasation.	the cardiovascular system
		(e.g., heart disease, congestive
		heart failure, hypertension,
		aortic stenosis,
		cardiomyopathy, valvular
		regurgitation, left ventricular
		dysfunction, atherosclerosis
		and atherosclerotic vascular

disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or as described below under "Cardiovascular Disorders").	Highly preferred indications include cardiovascular,	disorders (e.g., systemic	such ás diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,
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hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud's	phenomenom, aneurysms,	restenosis; venous and	Iymphatic disorders such as	

lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,

heart disease, cardiac arrest,	neart valve disease, and vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic	inflammatory diseases, e.g.,	inflammatory bowel disease	and Crohn's disease), and pain	management.	A highly preferred	embodiment of the invention	includes a method for	stimulating MIP1a production.	An alternative highly preferred	embodiment of the invention
																								MIP-1alpha FMAT. Assays	for immunomodulatory	proteins produced by activated	dendritic cells that upregulate	monocyte/macrophage and T	cell chemotaxis are well
																								Production of	MIP1alpha	1			
																								1203					
														•										HJMBT65					
								,						·-									, , , , , , , , , , , , , , , , , , , 		255		***		

	known in the art and may be	includes a method for
-	used or routinely modified to	inhibiting (e.g., reducing)
	assess the ability of	MIP1a production. A highly
	polypeptides of the invention	preferred indication is
-	(including antibodies and	infection (e.g., an infectious
	agonists or antagonists of the	disease as described below
	invention) to mediate	under "Infectious Disease").
	immunomodulation, modulate	Preferred indications include
	chemotaxis, and modulate T	blood disorders (e.g., as
	cell differentiation. Exemplary	described below under
	assays that test for	"Immune Activity", "Blood-
	immunomodulatory proteins	Related Disorders", and/or
	evaluate the production of	"Cardiovascular Disorders").
	chemokines, such as	Highly preferred indications
	macrophage inflammatory	include autoimmune diseases
	protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
	the activation of	systemic lupus erythematosis,
	monocytes/macrophages and T	multiple sclerosis and/or as
	cells. Such assays that may be	described below) and
	used or routinely modified to	immunodeficiencies (e.g., as
	test immunomodulatory and	described below). Additional
	chemotaxis activity of	highly preferred indications
	polypeptides of the invention	include inflammation and
	(including antibodies and	inflammatory disorders.
	agonists or antagonists of the	Preferred indications also
	invention) include assays	include anemia, pancytopenia,
	disclosed in Miraglia et al., J	leukopenia, thrombocytopenia,
	Biomolecular Screening 4:193-	Hodgkin's disease, acute
	204(1999); Rowland et al.,	lymphocytic anemia (ALL),
	"Lymphocytes: a practical	plasmacytomas, multiple
	approach" Chapter 6:138-160	myeloma, Burkitt's lymphoma,

				(2000): Satthanorn and	arthritis. AIDS oranulomatous
				Eremin, J R Coll Surg Ednb	disease, inflammatory bowel
				45(1):9-19 (2001); Drakes et	disease, sepsis, neutropenia,
				al., Transp Immunol 8(1):17-	neutrophilia, psoriasis,
				29 (2000); Verhasselt et al., J	suppression of immune
-10				Immunol 158:2919-2925	reactions to transplanted
				(1997); and Nardelli et al., J	organs and tissues, hemophilia,
				Leukoc Biol 65:822-828	hypercoagulation, diabetes
				(1999), the contents of each of	mellitus, endocarditis,
				which are herein incorporated	meningitis, Lyme Disease,
				by reference in its entirety.	asthma, and allergy.
				Human dendritic cells that may	Preferred indications also
				be used according to these	include neoplastic diseases
				assays may be isolated using	(e.g., leukemia, lymphoma,
				techniques disclosed herein or	and/or as described below
				otherwise known in the art.	under "Hyperproliferative
				Human dendritic cells are	Disorders"). Highly preferred
				antigen presenting cells in	indications include neoplasms
				suspension culture, which,	and cancers, such as, leukemia,
				when activated by antigen	lymphoma, prostate, breast,
				and/or cytokines, initiate and	lung, colon, pancreatic,
				upregulate T cell proliferation	esophageal, stomach, brain,
				and functional activities.	liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
255	HJMBT65	1203	CD71 in Human T cells		

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	Highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below), and	immunodeficiencies (e.g., as	described below). An	additional highly preferred	indication is infection (e.g.,	AIDS, and/or an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred
	Assays for the activation of	transcription through the	NFKB response element are	well-known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et
SEAP in ATP-3T3- L1	Activation of	transcription	through NFKB	response element in	immune cells (such	as T-cells).	`																						
1204	1204										us·																		
HJMBW30	HJMBW30	100 000						-10.																					-
256		256				-														_						-			

7 indications include neoplasms	and cancers, such	as,melanoma, renal cell		lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,		preferred indications include	benign dysproliferative	at disorders and pre-neoplastic	se conditions, such as, for			Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	suppression of immune	reactions to transplanted
al., Virus Gnes 15(2):105-117	(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.															
		a.													-				,											
	,																					-								

					organs, asthma and allergy.
256	HJMBW30	1204	SEAP in SW480		
((HJPAD75	1205	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
257			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
			Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
				the art and may be used or	(e.g., as described below under
				routinely modified to assess	"Immune Activity",
				the ability of polypeptides of	"Cardiovascular Disorders",
				the invention (including	and/or "Blood-Related
		1.		antibodies and agonists or	Disorders"), and infection
				antagonists of the invention) to	(e.g., an infectious disease as
				promote or inhibit immune cell	described below under
				(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
				activation, and apoptosis.	preferred indications include
				Exemplary assays for JNK and	autoimmune diseases (e.g.,
				p38 kinase activity that may be	rheumatoid arthritis, systemic
·				used or routinely modified to	lupus erythematosis, multiple
		•		test JNK and p38 kinase-	sclerosis and/or as described
				induced activity of	below) and
				polypeptides of the invention	immunodeficiencies (e.g., as
				(including antibodies and	described below). Additional
		<u>.</u>		agonists or antagonists of the	highly preferred indications
_				invention) include the assays	include inflammation and
				disclosed in Forrer et al., Biol	inflammatory disorders.
				Chem 379(8-9):1101-1110	Highly preferred indications
				(1998); Gupta et al., Exp Cell	also include neoplastic
			,	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
				Kyriakis JM, Biochem Soc	lymphoma, and/or as described

			C (4.70 40 (1000). Chang	[]
			3yinp 04:29-40 (1999), Citaing	Delow uluci
	- M		and Karin, Nature	"Hyperproliferative
			410(6824):37-40 (2001); and	Disorders"). Highly preferred
			Cobb MH, Prog Biophys Mol	indications include neoplasms
			Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
	-		the contents of each of which	lymphoma, prostate, breast,
		-	are herein incorporated by	lung, colon, pancreatic,
			reference in its entirety. T	esophageal, stomach, brain,
			cells that may be used	liver, and urinary cancer. Other
	<u>, </u>		according to these assays are	preferred indications include
	<u></u>		publicly available (e.g.,	benign dysproliferative
			through the ATCC).	disorders and pre-neoplastic
			Exemplary mouse T cells that	conditions, such as, for
•			may be used according to these	example, hyperplasia,
			assays include the CTLL cell	metaplasia, and/or dysplasia.
			line, which is an IL-2	Preferred indications include
			dependent suspension-culture	arthritis, asthma, AIDS,
			cell line with cytotoxic	allergy, anemia, pancytopenia,
			activity.	leukopenia, thrombocytopenia,
				Hodgkin"s disease, acute
				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt"s lymphoma,
	2.			granulomatous disease,
				inflammatory bowel disease,
	24			sepsis, psoriasis, suppression
	***			of immune reactions to
				transplanted organs and
			•	tissues, endocarditis,
-				meningitis, and Lyme Disease.
HJPAD75	1205	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred

257			by T cells and has strong	embodiment of the invention
			effects on B cells. IL-6	includes a method for
-			participates in IL-4 induced	stimulating (e.g., increasing)
			IgE production and increases	IL-6 production. An alternative
			IgA production (IgA plays a	highly preferred embodiment
	•		role in mucosal immunity).	of the invention includes a
			IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
			Deregulated expression of IL-6	reducing) IL-6 production. A
			has been linked to autoimmune	highly preferrred indication is
			disease, plasmacytomas,	the stimulation or enhancement
			myelomas, and chronic	of mucosal immunity. Highly
			hyperproliferative diseases.	preferred indications include
			Assays for immunomodulatory	blood disorders (e.g., as
			and differentiation factor	described below under
		_	proteins produced by a large	"Immune Activity", "Blood-
			variety of cells where the	Related Disorders", and/or
			expression level is strongly	"Cardiovascular Disorders"),
			regulated by cytokines, growth	and infection (e.g., as
			factors, and hormones are well	described below under
			known in the art and may be	"Infectious Disease"). Highly
			used or routinely modified to	preferred indications include
		-	assess the ability of	autoimmune diseases (e.g.,
			polypeptides of the invention	rheumatoid arthritis, systemic
			(including antibodies and	lupus erythematosis, multiple
			agonists or antagonists of the	sclerosis and/or as described
			invention) to mediate	below) and
		-	immunomodulation and	immunodeficiencies (e.g., as
			differentiation and modulate T	described below). Highly
		-	cell proliferation and function.	preferred indications also
			Exemplary assays that test for	include boosting a B cell-
			immunomodulatory proteins	mediated immune response

and alternatively suppressing a B cell-mediated immune response. Highly preferred indications include	inflammatory disorders. Additional highly preferred indications include	asthma and allergy. Highly preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma,	leukemia, lymphoma, melanoma, and/or as described below under	"Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, myeloma,	plasmacytoma, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and	urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include
evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell	promeration and iuncuonal activities. Such assays that may be used or routinely modified to test	immunomodulatory and diffferentiation activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J	Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160	(2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety.	Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in

anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infectious disease as described below under "Infectious Disease").		A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure,
suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.		Assays for the regulation of transcription through the FAS promoter element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and
	Glucose Production in H4IIE	Regulation of transcription through the FAS promoter element in hepatocytes
	1205	1205
	HJPAD75	HJPAD75
	257	257

nephropathy and/or other diseases and disorders as	described in the "Renal Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and
agonists or antagonists of the invention) to activate the FAS	promoter element in a reporter construct and to regulate	transcription of FAS, a key	enzyme for lipogenesis. FAS	promoter is regulated by many	transcription factors including	SREBP. Insulin increases FAS	gene transcription in livers of	diabetic mice. This	stimulation of transcription is	also somewhat glucose	dependent. Exemplary assays	that may be used or routinely	modified to test for FAS	promoter element activity (in	hepatocytes) by polypeptides	of the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Xiong, S., et al., Proc Natl	Acad Sci U.S.A., 97(8):3948-	53 (2000); Roder, K., et al.,	Eur J Biochem, 260(3):743-51	(1999); Oskouian B, et al.,	Biochem J, 317 (Pt 1):257-65	(1996); Berger, et al., Gene	66:1-10 (1988); and, Cullen,	B., et al., Methods in Enzymol.
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		-								-			_									-						

HJPAD75 1205 SEAP in HIB/CRE adipose cells (such as 3T3-L1 cells)

		A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell
example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127- 133 (1974), which is herein incorporated by reference in its entirety.		Caspase Apoptosis Rescue. Assays for caspase apoptosis rescue are well known in the art and may be used or routinely modified to assess the ability of the polypeptides of the invention (including antibodies and agonists or
	IFNg in Human T-cell 2B9	Protection from Endothelial Cell Apoptosis.
	1205	1206
	HJPAD75	HJPCP42
	257	258

	antagonists of the invention) to	growth. A highly preferred
	inhibit caspase protease-	embodiment of the invention
	mediated apoptosis.	includes a method for
	Exemplary assays for caspase	stimulating endothelial cell
	apoptosis that may be used or	proliferation. An alternative
	routinely modified to test	highly preferred embodiment
	caspase apoptosis rescue of	of the invention includes a
	polypeptides of the invention	method for inhibiting
	(including antibodies and	endothelial cell proliferation.
	agonists or antagonists of the	A highly preferred
	invention) include the assays	embodiment of the invention
	disclosed in Romeo et al.,	includes a method for
	Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
	(2000); Messmer et al., Br J	growth. An alternative highly
	Pharmacol 127(7): 1633-1640	preferred embodiment of the
	(1999); and J Atheroscler	invention includes a method
	Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
	the contents of each of which	growth. A highly preferred
	are herein incorporated by	embodiment of the invention
	reference in its entirety.	includes a method for
	Endothelial cells that may be	stimulating apoptosis of
	used according to these assays	endothelial cells. An
-	are publicly available (e.g.,	alternative highly preferred
	through commercial sources).	embodiment of the invention
	Exemplary endothelial cells	includes a method for
	that may be used according to	inhibiting (e.g., decreasing)
	these assays include bovine	apoptosis of endothelial cells.
	aortic endothelial cells	A highly preferred
	(bAEC), which are an example	embodiment of the invention
	of endothelial cells which line	includes a method for
	blood vessels and are involved	stimulating angiogenisis. An

alternative highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment		highly preferred embodiment of the invention includes a method for inducing cardiac	hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as	described below under "Hyperproliferative	Disorders"), and disorders of the cardiovascular system	(e.g., heart disease, congestive heart failure, hypertension,	aortic stenosis, cardiomyopathy, valvular	regurgitation, left ventricular dysfunction, atherosclerosis	and atherosclerotic vascular disease, diabetic nephropathy,	intracardiac shunt, cardiac hypertrophy, myocardial	infarction, chronic	nemodynamic overload, and/or as described below under
in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone,	and immune cell extravasation.											

"Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer,	such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma,

lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as,	prostate, oreast, rung, coron, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,	metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s	phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also
		1640	

include trauma such as wounds, burns, and injured tissue (e.g., vascular injury	such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis.	cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred	indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders,	age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest.	heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune

Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	
	This reporter assay measures activation or inhibition of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation or inhibition of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including
	Activation or inhibition of transcription through NFKB response element in immune cells (such as basophils).
	1206
	HJPCP42
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antibodies and agonists or antagonists of the invention) to regulate NFKB transcription	factors and modulate expression of immunomodulatory genes.	NFkB is important in the pathogenesis of asthma. Exemplary assays for	transcription through the NFKB response element that	may be used or rountinely modified to test NFKB-	response element activity of	polypeptides of the invention (including antibodies and	agonists or antagonists of the	invention) include assays	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Froc Natl Acad Sci USA 85:6342-6346 (1988); Marone	et al, Int Arch Allergy	Immunol 114(3):207-17	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Cells were pretreated with SID	supernatants or controls for 15-
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		A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a
18 hours, and then 10 ng/mL of TNF was added to stimulate the NFkB reporter. SEAP activity was measured after 48 hours. Basophils that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human basophil cell lines that may be used according to these assays include Ku812, originally established from a natient with	chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils. See, Kishi et al., Leuk Res. 9:381-390 (1985); Blom et al., Eur J Immunol. 22:2025-32 (1992), where the contents of each are herein incorporated by reference in its entirety.	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity).
		Production of IL-6
		1208
		НКААН36
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III6 induces cytotoxic T cells	method for inhibiting (e o
Deregulated expression of II6	reducing) II6 production. A
has been linked to autoimmune	highly preferred indication is
disease, plasmacytomas,	the stimulation or enhancement
myelomas, and chronic	of mucosal immunity. Highly
hyperproliferative diseases.	preferred indications include
Assays for immunomodulatory	blood disorders (e.g., as
and differentiation factor	described below under
proteins produced by a large	"Immune Activity", "Blood-
 variety of cells where the	Related Disorders", and/or
expression level is strongly	"Cardiovascular Disorders"),
regulated by cytokines, growth	and infection (e.g., as
factors, and hormones are well	described below under
known in the art and may be	"Infectious Disease"). Highly
used or routinely modified to	preferred indications include
assess the ability of	autoimmune diseases (e.g.,
polypeptides of the invention	rheumatoid arthritis, systemic
(including antibodies and	lupus erythematosis, multiple
agonists or antagonists of the	sclerosis and/or as described
invention) to mediate	below) and
immunomodulation and	immunodeficiencies (e.g., as
differentiation and modulate T	described below). Highly
cell proliferation and function.	preferred indications also
Exemplary assays that test for	include boosting a B cell-
immunomodulatory proteins	mediated immune response
evaluate the production of	and alternatively suppressing a
cytokines, such as IL-6, and	B cell-mediated immune
the stimulation and	response. Highly preferred
upregulation of T cell	indications include
proliferation and functional	inflammation and
activities. Such assays that	inflammatory

disorders. Additional highly preferred indications include asthma and allergy. Highly preferred indications include neoplastic diseases (e.g.,		"Hyperproliterative Disorders"). Highly preferred indications include neoplasms and cancers, such as, myeloma,	· · · · · · · · · · · · · · · · · · ·	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,	metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention	(including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J	Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160	Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety.	Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art.	Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.

granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include
	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immune cell activation.
	Production of MCP-1
	1208
	НКААН36
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Exemplary assays that test for	inflammation and
immunomodulatory proteins	inflammatory disorders.
evaluate the production of cell	Preferred indications include
surface markers, such as	blood disorders (e.g., as
monocyte chemoattractant	described below under
protein (MCP), and the	"Immune Activity", "Blood-
activation of monocytes and T	Related Disorders", and/or
cells. Such assays that may be	"Cardiovascular Disorders").
used or routinely modified to	Highly preferred indications
test immunomodulatory and	include autoimmune diseases
diffferentiation activity of	(e.g., rheumatoid arthritis,
polypeptides of the invention	systemic lupus erythematosis,
(including antibodies and	multiple sclerosis and/or as
agonists or antagonists of the	described below) and
invention) include assays	immunodeficiencies (e.g., as
disclosed in Miraglia et al., J	described below). Preferred
Biomolecular Screening 4:193-	indications also include
204(1999); Rowland et al.,	anemia, pancytopenia,
"Lymphocytes: a practical	leukopenia, thrombocytopenia,
approach" Chapter 6:138-160	Hodgkin's disease, acute
(2000); Satthaporn and	lymphocytic anemia (ALL),
Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
158:2919-2925 (1997), the	disease, inflammatory bowel
contents of each of which are	disease, sepsis, neutropenia,
herein incorporated by	neutrophilia, psoriasis,
 reference in its entirety.	suppression of immune
Human dendritic cells that may	reactions to transplanted
be used according to these	organs and tissues,
assays may be isolated using	hemophilia, hypercoagulation,

				techniques disclosed herein or	diabetes mellitus, endocarditis,
				otherwise known in the art.	meningitis (bacterial and
				Human dendritic cells are	viral), Lyme Disease, asthma,
				antigen presenting cells in	and allergy Preferred
				suspension culture, which,	indications also include
				when activated by antigen	neoplastic diseases (e.g.,
				and/or cytokines, initiate and	leukemia, lymphoma, and/or as
				upregulate T cell proliferation	described below under
				and functional activities.	"Hyperproliferative
					Disorders"). Highly preferred
					indications include neoplasms
					and cancers, such as, leukemia,
					lymphoma, prostate, breast,
					lung, colon, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
260	HKAAH36	1208	IgG in Human B cells SAC		
	HKAAK02	1209	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
261				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a

method for inhibiting (e.g.,	highly preferred indication is	the stimulation or enhancement	of mucosal immunity. Highly	preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response	and alternatively suppressing a	B cell-mediated immune	response. Highly preferred	indications include	inflammation and	inflammatory
IL-6 induces cytotoxic T cells.	has been linked to autoimmune	disease, plasmacytomas,	myelomas, and chronic	hyperproliferative diseases.	Assays for immunomodulatory	and differentiation factor	proteins produced by a large	variety of cells where the	expression level is strongly	regulated by cytokines, growth	factors, and hormones are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and	the stimulation and	upregulation of T cell	proliferation and functional	activities. Such assays that
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may be used or routinely	disorders.Additional highly
modified to test	preferred indications include
 immunomodulatory and	asthma and allergy. Highly
 diffferentiation activity of	preferred indications include
polypeptides of the invention	neoplastic diseases (e.g.,
 (including antibodies and	myeloma, plasmacytoma,
 agonists or antagonists of the	leukemia, lymphoma,
invention) include assays	melanoma, and/or as described
disclosed in Miraglia et al., J	below under
Biomolecular Screening 4:193-	"Hyperproliferative
204(1999); Rowland et al.,	Disorders"). Highly preferred
 "Lymphocytes: a practical	indications include neoplasms
approach" Chapter 6:138-160	and cancers, such as, myeloma,
(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
Immunol 158:2919-2925	lymphoma, melanoma, and
(1997), the contents of each of	prostate, breast, lung, colon,
 which are herein incorporated	pancreatic, esophageal,
by reference in its entirety.	stomach, brain, liver and
Human dendritic cells that may	urinary cancer. Other preferred
 be used according to these	indications include benign
assays may be isolated using	dysproliferative disorders and
 techniques disclosed herein or	pre-neoplastic conditions, such
otherwise known in the art.	as, for example, hyperplasia,
Human dendritic cells are	metaplasia, and/or dysplasia.
 antigen presenting cells in	Preferred indications include
suspension culture, which,	anemia, pancytopenia,
 when activated by antigen	leukopenia, thrombocytopenia,
and/or cytokines, initiate and	Hodgkin's disease, acute
 upregulate T cell proliferation	lymphocytic anemia (ALL),
and functional activities.	multiple myeloma, Burkitt's
	lymphoma, arthritis, AIDS,

granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include
	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immune cell activation.
	Production of MCP-1
	1209
	HKAAK02
	261

			otherwise known in the art.	meningitis (bacterial and
			Human dendritic cells are antigen presenting cells in	viral), Lyme Disease, asthma, and allergy Preferred
			suspension culture, which,	indications also include
			when activated by antigen	neoplastic diseases (e.g.,
			and/or cytokines, initiate and	leukemia, lymphoma, and/or as
			upregulate T cell proliferation	described below under
			and functional activities.	"Hyperproliferative
				Disorders"). Highly preferred
				indications include neoplasms
				and cancers, such as, leukemia,
				lymphoma, prostate, breast,
				lung, colon, pancreatic,
				esophageal, stomach, brain,
				liver, and urinary cancer. Other
				preferred indications include
				benign dysproliferative
				disorders and pre-neoplastic
				conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
HKABI84	1210	Endothelial Cell	Caspase Apoptosis. Assays for	A highly preferred
		Apoptosis	caspase apoptosis are well	embodiment of the invention
 ,			known in the art and may be	includes a method for
			used or routinely modified to	stimulating endothelial cell
			assess the ability of	growth. An alternative highly
			polypeptides of the invention	preferred embodiment of the
			(including antibodies and	invention includes a method
		,	agonists or antagonists of the	for inhibiting endothelial cell
			invention) to promote caspase	growth. A highly preferred

embodiment of the invention	includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	endothelial cell proliferation.	A highly preferred	embodiment of the invention	includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment
protease-mediated apoptosis.	Induction of apoptosis in	endothelial cells supporting the	vasculature of tumors is	associated with tumor	regression due to loss of tumor	blood supply. Exemplary	assays for caspase apoptosis	that may be used or routinely	modified to test capase	apoptosis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Lee et al., FEBS	Lett 485(2-3): 122-126 (2000);	Nor et al., J Vasc Res 37(3):	209-218 (2000); and Karsan	and Harlan, J Atheroscler	Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine
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of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under	"Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis,	cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial	infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular,	endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the
aortic endothelial cells (bAEC), which are an example of endothelial cells which line blood vessels and are involved in functions that include, but are not limited to,	angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.			
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indications include benign dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,
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		cerebrovascular disease, renal
		diseases such as acute renal
		failure, and osteoporosis.
		Additional highly preferred
		indications include stroke,
	 	graft rejection, diabetic or
		other retinopathies, thrombotic
		and coagulative disorders,
		vascularitis, lymph
		angiogenesis, sexual disorders,
		age-related macular
		degeneration, and treatment
		/prevention of endometriosis
		and related conditions.
		Additional highly preferred
	 	indications include fibromas,
		heart disease, cardiac arrest,
		heart valve disease, and
		vascular disease.
		Preferred indications include
	 	blood disorders (e.g., as
		described below under
		"Immune Activity", "Blood-
		Related Disorders", and/or
		"Cardiovascular Disorders").
		Preferred indications include
_		autoimmune diseases (e.g.,
		rheumatoid arthritis, systemic
		lupus erythematosis, multiple
		sclerosis and/or as described
		below) and

HKABI84 1210 Activation of transcription through NFAT response in immune cells (such as T-cells).
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ion additional highly preferred	indication is infection (e.g., an	the infectious disease as described	below under "Infectious	Gene Disease"). Preferred		ol diseases (e.g., leukemia,		USA below under	fling "Hyperproliferative	-	30er indications include neoplasms	3iol and cancers, such as, for		ol and prostate, breast, lung,	l colon, pancreatic, esophageal,	stomach, brain, liver and	93), urinary cancer. Other preferred	ich indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,		Preferred indications also	include anemia, pancytopenia,	_	these Hodgkin's disease, acute	VT lymphocytic anemia (ALL),	nsion plasmacytomas, multiple		ated. arthritis, AIDS, granulomatous
polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Serfling	et al., Biochim Biophys Acta	1498(1):1-18 (2000); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the JURKAT	cell line, which is a suspension	culture of leukemia cells that	produce IL-2 when stimulated.
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of of tion						disease, inflammatory bowel
Activation of transcription through the through NFKB response element are response element in well-known in the art and may immune cells (such as T-cells). Polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB. Fresponse element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and modified to test NFKB.						disease, sepsis, neutropenia, neutrophilia, psoriasis,
Activation of transcription through the through NFKB response element are response element in well-known in the art and may immune cells (such as T-cells). Polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB. Fresponse element activity of polypeptides of the invention (including antibodies and agonities and modified to test NFKB.						suppression of immune
transcription through NFKB response element in immune cells (such as T-cells). polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB- response element activity of polypeptides of the invention						reactions to transplanted
transcription through NFKB response element in well-known in the art and may immune cells (such be used or routinely modified as T-cells). polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and including antibodies antibodies and including antibodies and including antibodie						organs and tissues,
transcription transcription transcription through NFKB response element in immune cells (such as T-cells). polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB- response element activity of polypeptides of the invention (including antibodies and						hemophilia, hypercoagulation,
Activation of transcription through the transcription through NFKB transcription through the transcription through the transcription through the imperator of the transcription through the imperator of the transcription through the immune cells (such as the all the act and may the immune cells (such as the ability of the assess the ability of including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that im may be used or rountinely an response element activity of in fincluding antibodies and difficulting antibodies and diffincluding antibodies and diffincluding antibodies and diffincluding antibodies and diffincluding antibodies and difficulting antibodies and difficulting antibodies and diffincluding antibo						diabetes mellitus, endocarditis,
Activation of transcription through the transcription through NFKB response element are response element in well-known in the art and may himmune cells (such as T-cells). De used or routinely modified in to assess the ability of as polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB Hamoulate expression of modulate expression of transcription factors and modulate expression of transcription through the down NFKB response element that in may be used or rountinely an response element activity of including antibodies and diffincluding antibodies and difficulting antibodies and diffincluding antibodies and diffinclu						meningitis, Lyme Disease,
transcription transcription transcription through NFKB response element are response element in well-known in the art and may H immune cells (such be used or routinely modified in as T-cells). polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB H transcription factors and inmunomodulatory genes. Exemplary assays for transcription through the down transcription through the down modified to test NFKB- are response element that in may be used or rountinely and response element activity of including antibodies and dincluding antibodies and						asthma and allergy.
transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and	 	HKABI84	1210	Activation of	Assays for the activation of	Highly preferred indications
NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and				transcription	transcription through the	include inflammation and
well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and				through NFKB	NFKB response element are	inflammatory disorders.
be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and				response element in	well-known in the art and may	Highly preferred indications
to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and				immune cells (such	be used or routinely modified	include blood disorders (e.g.,
				as T-cells).	to assess the ability of	as described below under
					polypeptides of the invention	"Immune Activity", "Blood-
					(including antibodies and	Related Disorders", and/or
					agonists or antagonists of the	"Cardiovascular Disorders").
					invention) to regulate NFKB	Highly preferred indications
					transcription factors and	include autoimmune diseases
					modulate expression of	(e.g., rheumatoid arthritis,
					immunomodulatory genes.	systemic lupus erythematosis,
					Exemplary assays for	multiple sclerosis and/or as
					transcription through the	described below), and
					NFKB response element that	immunodeficiencies (e.g., as
					may be used or rountinely	described below). An
					modified to test NFKB-	additional highly preferred
					response element activity of	indication is infection (e.g.,
					polypeptides of the invention	AIDS, and/or an infectious
					(including antibodies and	disease as described below

					disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.
E92	HKABZ65	1211	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and increases lgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include

	polypeptides of the invention	rheumatoid arthritis, systemic
	(including antibodies and	lupus erythematosis, multiple
•	agonists or antagonists of the	sclerosis and/or as described
	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
 	differentiation and modulate T	described below). Highly
	cell proliferation and function.	preferred indications also
	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response
	evaluate the production of	and alternatively suppressing a
	cytokines, such as IL-6, and	B cell-mediated immune
	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
	may be used or routinely	disorders.Additional highly
	modified to test	preferred indications include
 	immunomodulatory and	asthma and allergy. Highly
	differentiation activity of	preferred indications include
 	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
-	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
 	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
 	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,

pancreatic, esophageal, stomach, brain, liver and	urinary cancer. Other preferred indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, and Lyme Disease.	An additonal preferred	indication is infection (e.g., an	infectious disease as described	below under "Infectious	Disease").	A highly preferred
which are herein incorporated by reference in its entirety.	Human dendritic cells that may be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.											-						Kinase assay. JNK and p38
																												Activation of
																												1211
							· ·																					HKABZ65
											_																	

	Endothelial Cell	kinase assays for signal	embodiment of the invention
	p38 or JNK	transduction that regulate cell	includes a method for
	Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
		apoptosis are well known in	growth. An alternative highly
		the art and may be used or	preferred embodiment of the
		routinely modified to assess	invention includes a method
		the ability of polypeptides of	for inhibiting endothelial cell
		the invention (including	growth. A highly preferred
		antibodies and agonists or	embodiment of the invention
		antagonists of the invention) to	includes a method for
		promote or inhibit cell	stimulating endothelial cell
		proliferation, activation, and	proliferation. An alternative
 		apoptosis. Exemplary assays	highly preferred embodiment
		for JNK and p38 kinase	of the invention includes a
		activity that may be used or	method for inhibiting
		routinely modified to test JNK	endothelial cell proliferation.
		and p38 kinase-induced	A highly preferred
		activity of polypeptides of the	embodiment of the invention
		invention (including antibodies	includes a method for
		and agonists or antagonists of	stimulating apoptosis of
		the invention) include the	endothelial cells. An
		assays disclosed in Forrer et	alternative highly preferred
		al., Biol Chem 379(8-9):1101-	embodiment of the invention
		1110 (1998); Gupta et al., Exp	includes a method for
		Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
		(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
		Soc Symp 64:29-48 (1999);	A highly preferred
		Chang and Karin, Nature	embodiment of the invention
		410(6824):37-40 (2001); and	includes a method for
		Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
		Biol 71(3-4):479-500 (1999);	endothelial cell activation. An

	ays s	chuman stimulating angiogenisis. An othelial cells alternative highly preferred embodiment of the invention includes a method for sls, and are inhibiting angiogenesis. A highly preferred embodiment		hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system	(e.g., heart disease, congestive heart failure, hypertension, aortic stenosis,
the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be	used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to	these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that	include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.		

cardiomyopathy, valvular	v. valvular
regurgitation. left ventricular	eft ventricular
dysfunction, atherosclerosis	herosclerosis
and atherosclerotic vascular	otic vascular
disease, diabetic nephropathy,	c nephropathy,
intracardiac shunt, cardiac	ınt, cardiac
hypertrophy, myocardial	lyocardial
infarction, chronic	nic
hemodynamic	hemodynamic overload, and/or
as described below under	low under
("Cardiovascular Disorders")	r Disorders").
Highly preferred indications	ed indications
include cardiovascular,	vascular,
endothelial and/or angiogenic	/or angiogenic
disorders (e.g., systemic	systemic
disorders that affect vessels	iffect vessels
such as diabetes mellitus, as	s mellitus, as
well as diseases of the vessels	s of the vessels
themselves, such as of the	ch as of the
arteries, capillaries, veins	ries, veins
and/or lymphatics). Highly	ics). Highly
preferred are indications that	dications that
 stimulate angiogenesis and/or	genesis and/or
 cardiovascularization. Highly	zation. Highly
preferred are indications that	dications that
inhibit angiogenesis and/or	nesis and/or
cardiovascularization.	ization.
Highly preferred indications	ed indications
include antiang	include antiangiogenic activity
to treat solid tumors,	mors,
leukemias, and Kaposi"s	Kaposi"s

Sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi"s sarcoma,	hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma,	angiosarcoma, haemangiopericytoma, lymphangiosarcoma. Highly	preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications	also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s

phenomenom, aneurysms, restenosis: venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment
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	,																												

					Invariantion of and amothicsis
					and related conditions.
					Additional highly preferred
					indications include fibromas,
-			-		heart disease, cardiac arrest,
					heart valve disease, and
					vascular disease.
_					Preferred indications include
					blood disorders (e.g., as
					described below under
					"Immune Activity", "Blood-
					Related Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
	_				described below). Additional
		-			preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HKABZ65	1211	Regulation of	Caspase Apoptosis. Assays	A highly preferred
263			apoptosis in	for caspase apoptosis are well	indication is diabetes mellitus.

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	pancreatic beta	known in the art and may be	An additional highly preferred
	cells.	used or routinely modified to	indication is a complication
		assess the ability of	associated with diabetes (e.g.,
		polypeptides of the invention	diabetic retinopathy, diabetic
		(including antibodies and	nephropathy, kidney disease
		agonists or antagonists of the	(e.g., renal failure,
		invention) to promote caspase	nephropathy and/or other
		protease-mediated apoptosis.	diseases and disorders as
		Apoptosis in pancreatic beta is	described in the "Renal
		associated with induction and	Disorders" section below),
		progression of diabetes.	diabetic neuropathy, nerve
		Exemplary assays for caspase	disease and nerve damage
		apoptosis that may be used or	(e.g., due to diabetic
		routinely modified to test	neuropathy), blood vessel
		capase apoptosis activity of	blockage, heart disease, stroke,
		polypeptides of the invention	impotence (e.g., due to diabetic
		(including antibodies and	neuropathy or blood vessel
		agonists or antagonists of the	blockage), seizures, mental
		invention) include the assays	confusion, drowsiness,
		disclosed in: Loweth, AC, et	nonketotic hyperglycemic-
		al., FEBS Lett, 400(3):285-8	hyperosmolar coma,
		(1997); Saini, KS, et al.,	cardiovascular disease (e.g.,
		Biochem Mol Biol Int,	heart disease, atherosclerosis,
		39(6):1229-36 (1996);	microvascular disease,
***		Krautheim, A., et al., Br J	hypertension, stroke, and other
		Pharmacol, 129(4):687-94	diseases and disorders as
		(2000); Chandra J, et al.,	described in the
		Diabetes, 50 Suppl 1:S44-7	"Cardiovascular Disorders"
		(2001); Suk K, et al., J	section below), dyslipidemia,
		Immunol, 166(7):4481-9	endocrine disorders (as
		(2001); Tejedo J, et al., FEBS	described in the "Endocrine

Disorders" section below),	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Aditional	highly preferred indications are	complications associated with	insulin resistance.									
Lett, 459(2):238-43 (1999); Zhang S. et al. FFBS Lett	455(3):315-20 (1999); Lee et	al., FEBS Lett 485(2-3): 122-	126 (2000); Nor et al., J Vasc	Res 37(3): 209-218 (2000);	and Karsan and Harlan, J	Atheroscler Thromb 3(2): 75-	80 (1996); the contents of each	of which are herein	incorporated by reference in its	entirety. Pancreatic cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC)	and/or may be routinely	generated. Exemplary	pancreatic cells that may be	used according to these assays	include RIN-m. RIN-m is a	rat adherent pancreatic beta	cell insulinoma cell line	derived from a radiation	induced transplantable rat islet	cell tumor. The cells produce	and secrete islet polypeptide	hormones, and produce insulin,	somatostatin, and possibly	glucagon. ATTC: #CRL-2057	Chick et al. Proc. Natl. Acad.	Sci. 1977 74:628; AF et al.
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				Proc. Natl. Acad. Sci. 1980	
770	HKACB56	1212	Myoblast cell	Assays for muscle cell	Highly preferred indications
704			proliferation	proliferation are well known in	include diabetes, myopathy,
				tile art and may be used or routinely modified to assess	muscle (such as.
		-		the ability of polypeptides of	rhabdomyoma, and
				the invention (including	rhabdosarcoma),
		4.0		antibodies and agonists or	cardiovascular disorders (such
				antagonists of the invention) to	as congestive heart failure,
				stimulate or inhibit myoblast	cachexia, myxomas, fibromas,
				cell proliferation. Exemplary	congenital cardiovascular
				assays for myoblast cell	abnormalities, heart disease,
				proliferation that may be used	cardiac arrest, heart valve
				or routinely modified to test	disease, vascular disease, and
				activity of polypeptides and	also as described below under
				antibodies of the invention	"Cardiovascular Disorders"),
				(including agonists or	stimulating myoblast
				antagonists of the invention)	proliferation, and inhibiting
				include, for example, assays	myoblast proliferation.
				disclosed in: Soeta, C., et al.	
				"Possible role for the c-ski	
				gene in the proliferation of	
				myogenic cells in regenerating	
				skeletal muscles of rats" Dev	
				Growth Differ Apr;43(2):155-	
			٠	64 (2001); Ewton DZ, et al.,	
				"IGF binding proteins-4, -5	
				and -6 may play specialized	
				roles during L6 myoblast	
				proliferation and	

HKACB56

				eosinophils that stimulate	production. An alternative
				eosinophil function and B cell	highly preferred embodiment
				Ig production and promote	of the invention includes a
				polarization of CD4+ cells into	method for stimulating (e.g.,
				TH2 cells are well known in	increasing) IL-5 production.
		-	•	the art and may be used or	A highly preferred
				routinely modified to assess	embodiment of the invention
				the ability of polypeptides of	includes a method for
				the invention (including	stimulating (e.g., increasing)
				antibodies and agonists or	immunoglobulin production.
		-		antagonists of the invention) to	An alternative highly preferred
				mediate immunomodulation,	embodiment of the invention
				stimulate immune cell	includes a method for
				function, modulate B cell Ig	inhibiting (e.g., decreasing)
				production, modulate immune	immunoglobulin production.
				cell polarization, and/or	A highly preferred indication
-				mediate humoral or cell-	includes allergy. A highly
				mediated immunity.	preferred indication includes
	•			Exemplary assays that test for	asthma. A highly preferred
				immunomodulatory proteins	indication includes rhinitis.
		-		evaluate the production of	An additional highly preferred
				cytokines, such as IL-5, and	indication is infection (e.g., an
				the stimulation of eosinophil	infectious disease as described
				function and B cell Ig	below under "Infectious
				production. Such assays that	Disease"), and inflammation
				may be used or routinely	and inflammatory disorders.
		•		modified to test	Preferred indications include
				immunomodulatory activity of	blood disorders (e.g., as
				polypeptides of the invention	described below under
				(including antibodies and	"Immune Activity", "Blood-
				agonists or antagonists of the	Related Disorders", and/or

		invention) include the assays	"Cardiovascular Disorders").
		disclosed in Miraolia et al	Preferred indications include
		Biomolecular Screening 4.103.	autoimmine diseases (e o
		Diolifocculai Delectining 7:173	date in the state of the state
		204 (1999); Kowland et al.,	rneumatoid arthritis, systemic
		"Lymphocytes: a practical	lupus erythematosis, multiple
		approach" Chapter 6:138-160	sclerosis and/or as described
		(2000); Ohshima et al., Blood	below) and
	-	92(9):3338-3345 (1998); Jung	immunodeficiencies (e.g., as
		et al., Eur J Immunol	described below). Preferred
		25(8):2413-2416 (1995); Mori	indications include neoplastic
		et al., J Allergy Clin Immunol	diseases (e.g., leukemia,
		106(1 Pt 2):558-564 (2000);	lymphoma, melanoma, and/or
		and Koning et al., Cytokine	as described below under
		9(6):427-436 (1997), the	"Hyperproliferative
		contents of each of which are	Disorders"). Preferred
		herein incorporated by	indications include neoplasms
		reference in its entirety.	and cancers, such as, leukemia,
		Human T cells that may be	lymphoma, melanoma, and
		used according to these assays	prostate, breast, lung, colon,
		may be isolated using	pancreatic, esophageal,
		techniques disclosed herein or	stomach, brain, liver and
-		otherwise known in the art.	urinary cancer. Other preferred
		Human T cells are primary	indications include benign
		human lymphocytes that	dysproliferative disorders and
		mature in the thymus and	pre-neoplastic conditions, such
		express a T cell receptor and	as, for example, hyperplasia,
		CD3, CD4, or CD8. These	metaplasia, and/or dysplasia.
		cells mediate humoral or cell-	Preferred indications include
		mediated immunity and may	anemia, pancytopenia,
		be preactivated to enhance	leukopenia, thrombocytopenia,
		responsiveness to	leukemias, Hodgkin's disease,

				immunomodulatory factors.	acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, menlitus, and Lyme Disease.
264	HKACB56	1212	IFNg in Human T- cell 2B9		
264	HKACB56	1212	Activation of Endothelial Cell p38 or JNK Signaling Pathway.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention of the invention includes a

	activity that may be used or	method for inhibiting
	routinely modified to test JNK	endothelial cell proliferation.
	and p38 kinase-induced	A highly preferred
	activity of polypeptides of the	embodiment of the invention
	invention (including antibodies	includes a method for
	and agonists or antagonists of	stimulating apoptosis of
	the invention) include the	endothelial cells. An
•	assays disclosed in Forrer et	alternative highly preferred
	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
	are herein incorporated by	embodiment of the invention
	reference in its entirety.	includes a method for
	Endothelial cells that may be	inhibiting (e.g., decreasing) the
	used according to these assays	activation of and/or
	are publicly available (e.g.,	inactivating endothelial cells.
	through the ATCC).	A highly preferred
	Exemplary endothelial cells	embodiment of the invention
	that may be used according to	includes a method for
	these assays include human	stimulating angiogenisis. An
	umbilical vein endothelial cells	alternative highly preferred
	(HUVEC), which are	embodiment of the invention
	endothelial cells which line	includes a method for
	venous blood vessels, and are	inhibiting angiogenesis. A

highly preferred embodiment of the invention includes a method for reducing cardiac	hypertrophy. An alternative highly preferred embodiment	of the invention includes a	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliterative	Disorders), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic
involved in functions that include, but are not limited to, anoiogenesis, vascular	permeability, vascular tone, and immune cell extravasation.																									
			,																							
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			discondance (a or accordance
	 		disolited (c.g., systemic
			disorders that affect vessels
	 		such as diabetes mellitus, as
			well as diseases of the vessels
			themselves, such as of the
	 		arteries, capillaries, veins
			and/or lymphatics). Highly
			preferred are indications that
	 		stimulate angiogenesis and/or
_			cardiovascularization. Highly
			preferred are indications that
	 		inhibit angiogenesis and/or
	 	,	cardiovascularization.
			Highly preferred indications
			include antiangiogenic activity
			to treat solid tumors,
			leukemias, and Kaposi"s
			sarcoma, and retinal disorders.
		 -	Highly preferred indications
			include neoplasms and cancer,
			such as, Kaposi"s sarcoma,
-			hemangioma (capillary and
			cavernous), glomus tumors,
	 		telangiectasia, bacillary
			angiomatosis,
			hemangioendothelioma,
			angiosarcoma,
	 •		haemangiopericytoma,
			lymphangioma,
			lymphangiosarcoma. Highly
			preferred indications also

include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from
											-							1,0												
											-					,														

balloon angioplasty, and	implant fixation scarring	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include
								-					-																
												-																	

autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	
	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cellmediate humoral or cellmediated immunity.
	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1212
	HKACB56
	264

immunomodulatory proteins	evaluate the production of	cytokilles, sucil as ICAIN LES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to
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	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include inflammation and inflammatory disorders, immunological disorders, neoplastic disorders (e.g. cancer/tumorigenesis), and cardiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders", "Hyperproliferative Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include neoplasms and cancers such as, for example, leukemia, lymphoma,
these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary
	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1212
	HKACB56
	7606

				endothelial cells that may be	melanoma, renal cell
				used according to these assays	carcinoma, and prostate,
				include human umbilical vein	breast, lung, colon, pancreatic,
				endothelial cells (HUVEC),	esophageal, stomach, brain,
				which are available from	liver and urinary cancer. Other
				commercial sources. The	preferred indications include
				expression of VCAM	benign dysproliferative
				(CD106), a membrane-	disorders and pre-neoplastic
				associated protein, can be	conditions, such as, for
		-		upregulated by cytokines or	example, hyperplasia,
				other factors, and contributes	metaplasia, and/or dysplasia.
				to the extravasation of	
				lymphocytes, leucocytes and	
				other immune cells from blood	
				vessels; thus VCAM	
				expression plays a role in	
				promoting immune and	
				inflammatory responses.	The state of the s
264	HKACB56	1212	SEAP in SW480		
	HKACD58	1213	Regulation of	Assays for the regulation of	A highly preferred indication
265	,		transcription via	transcription through the	is diabetes mellitus.
			DMEF1 response	DMEF1 response element are	Additional highly preferred
			element in	well-known in the art and may	indications include
			adipocytes and pre-	be used or routinely modified	complications associated with
			adipocytes	to assess the ability of	diabetes (e.g., diabetic
				polypeptides of the invention	retinopathy, diabetic
				(including antibodies and	nephropathy, kidney disease
				agonists or antagonists of the	(e.g., renal failure,
				invention) to activate the	nephropathy and/or other
				DMEF1 response element in a	diseases and disorders as

	reporter construct (such as that	described in the "Renal
	containing the GLUT4	Disorders" section below),
	promoter) and to regulate	diabetic neuropathy, nerve
	insulin production. The	disease and nerve damage
	DMEF1 response element is	(e.g., due to diabetic
_	present in the GLUT4	neuropathy), blood vessel
	promoter and binds to MEF2	blockage, heart disease, stroke,
	transcription factor and another	impotence (e.g., due to diabetic
	transcription factor that is	neuropathy or blood vessel
	required for insulin regulation	blockage), seizures, mental
	of Glut4 expression in skeletal	confusion, drowsiness,
	muscle. GLUT4 is the primary	nonketotic hyperglycemic-
	insulin-responsive glucose	hyperosmolar coma,
	transporter in fat and muscle	cardiovascular disease (e.g.,
	tissue. Exemplary assays that	heart disease, atherosclerosis,
	may be used or routinely	microvascular disease,
_	modified to test for DMEF1	hypertension, stroke, and other
	response element activity (in	diseases and disorders as
	adipocytes and pre-adipocytes)	described in the
	by polypeptides of the	"Cardiovascular Disorders"
	invention (including antibodies	section below), dyslipidemia,
	and agonists or antagonists of	endocrine disorders (as
	the invention) include assays	described in the "Endocrine
	disclosed inThai, M.V., et al., J	Disorders" section below),
	Biol Chem, 273(23):14285-92	neuropathy, vision impairment
	(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
	Chem, 275(21):16323-8	blindness), ulcers and impaired
	(2000); Liu, M.L., et al., J Biol	wound healing, and infection
	Chem, 269(45):28514-21	(e.g., infectious diseases and
	(1994); "Identification of a 30-	disorders as described in the
	base pair regulatory element	"Infectious Diseases" section

and novel DNA binding below, especially of the protein that regulates the human GLUT4 promoter in transgenic mice,", J Biol Chem. 2000 Aug 4,275(21),2366-73; complications associated with Berger, et al., Gene 66.1-10 (2000 Aug 4,275(21),2366-73; complications associated with Berger, et al., Gene 66.1-10 (2000 Aug 4,275(21),2366-73; complications include Methods in Enzymol. Weight loss or alternatively, 216:362-368 (1992), the comported by complexity and pre-adipocytes and pre-adipocyte and adipocyte of line. Mouse 313-1. cell inches which is an adherent mouse preadipocyte cell line. Mouse 313-1. cells are a continuous substrain of 313 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipocyte to adipocyte to adipocyte conditions.																															
and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:32–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 373-L1 cell line. Mouse 373-L1 cell line mouse preadipocyte cell line. Mouse 373-L1 cells are a continuous substrain of 373 fibroblasts developed through clonal isolation. These cells undergoe a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.	below, especially of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional highly	preferred indications are	complications associated with	insulin resistance.																			
	and novel DNA binding	protein that regulates the	human GLUT4 promoter in	transgenic mice", J Biol Chem.	2000 Aug 4;275(31):23666-73;	Berger, et al., Gene 66:1-10	(1988); and, Cullen, B., et al.,	Methods in Enzymol.	216:362–368 (1992), the	contents of each of which is	herein incorporated by	reference in its entirety.	Adipocytes and pre-adipocytes	that may be used according to	these assays are publicly	available (e.g., through the	ATCC) and/or may be	routinely generated.	Exemplary cells that may be	used according to these assays	include the mouse 3T3-L1 cell	line which is an adherent	mouse preadipocyte cell line.	Mouse 3T3-L1 cells are a	continuous substrain of 3T3	fibroblasts developed through	clonal isolation. These cells	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	culture conditions.
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	HKACD58	1213	IL-2 in Human T		
265			cells		
	HKACD58	1213	Activation of	Assays for the activation of	A preferred embodiment of
265			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
-				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
-				66:1-10 (1998); Cullen and	immune response, and
				Malm, Methods in Enzymol	suppressing a T cell-mediated
				216:362-368 (1992); Henthorn	immune response. Additional
				et al., Proc Natl Acad Sci USA	highly preferred indications

include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,
85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.														
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					Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
265	НКАСD58	1213	Caspase (+camptothecin) in SW480		under miechous Disease).
265	HKACD58	1213	Caspase (+paclitaxel) in SW480		
266	HKACH44	1214	Activation of Endothelial Cell p38 or JNK Signaling Pathway.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly

		the art and may be used or	nreferred embodiment of the
		routinely modified to assess	invention includes a method
		the ability of polypeptides of	for inhibiting endothelial cell
		the invention (including	growth. A highly preferred
		antibodies and agonists or	embodiment of the invention
		antagonists of the invention) to	includes a method for
		promote or inhibit cell	stimulating endothelial cell
		proliferation, activation, and	proliferation. An alternative
		apoptosis. Exemplary assays	highly preferred embodiment
		for JNK and p38 kinase	of the invention includes a
		activity that may be used or	method for inhibiting
		routinely modified to test JNK	endothelial cell proliferation.
		and p38 kinase-induced	A highly preferred
		activity of polypeptides of the	embodiment of the invention
		invention (including antibodies	includes a method for
		and agonists or antagonists of	stimulating apoptosis of
P. W. P.		the invention) include the	endothelial cells. An
		assays disclosed in Forrer et	alternative highly preferred
		al., Biol Chem 379(8-9):1101-	embodiment of the invention
		1110 (1998); Gupta et al., Exp	includes a method for
		Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
		(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
		Soc Symp 64:29-48 (1999);	A highly preferred
		Chang and Karin, Nature	embodiment of the invention
		410(6824):37-40 (2001); and	includes a method for
		Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
		Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
		the contents of each of which	alternative highly preferred
		are herein incorporated by	embodiment of the invention
		reference in its entirety.	includes a method for
		Endothelial cells that may be	inhibiting (e.g., decreasing) the

activation of and/or inactivating endothelial cells. A highly preferred embodiment of the invention includes a method for	stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a	method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis
used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to	these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to	angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.
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disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,
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hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,

lymphangitis, and lymphedema; and other vascular disorders such as	peripheral vascular disease, and cancer. Highly preferred indications also	include trauma such as wounds, burns, and injured tissue (e.g., vascular injury	such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions),	implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis,	cerebrovascular disease, renal diseases such as acute renal	failure, and osteoporosis. Additional highly preferred indications include stroke,	graft rejection, diabetic or other retinopathies, thrombotic	and coagulative disorders, vascularitis, lymph	angiogenesis, sexual disorders, age-related macular	degeneration, and treatment /prevention of endometriosis	and related conditions. Additional highly preferred indications include fibromas,
lymphan lymphede vascular	periphera and canc preferred	include the wounds, tissue (e.	such as, i balloon a atherosch	implant fischemia	cerebrov	failure, a Addition indication	graft reje other reti	and coag vasculari	angiogen age-relat	degenera /preventi	and relat Addition indicatio
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heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.		Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammation, and
		Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element
	DT-ATP in DT-ATP-SW480	Activation of transcription through GAS response element in
	1215	1215
	НКАСМ93	НКАСМ93
	267	267

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orders.	preferred	le immune	c disorders	d below un	v", and)isorders").	ases (e.g.,	tis, system	sis, Crohn'	sclerosis	ed below),	ies (e.g., a	, boosting	ted immun	ernatively,	-lihqonise	e response.													
inflammatory disorders.	Additional highly preferred	indications include immune	and hematopoietic disorders	(e.g., as described below under	"Immune Activity", and	"Blood-Related Disorders"),	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, Crohn's	disease, multiple sclerosis	and/or as described below),	immunodeficiencies (e.g., as	described below), boosting an	eosinophil-mediated immune	response and, alternatively,	suppressing an eosinophil-	mediated immune response.													
inflam	Additi	indica	and he	(e.g.,	"Imm"	"Bloo	autoin	rheum	lupus	diseas	and/o	immn	descri	eosino	respor	suppr	media			,				_						
are well-known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	gene expression (commonly	via STAT transcription factors)	involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	:1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995); the	1
are we	may b	modifi	of poly	invent	and ag	the inv	gene	via ST	involv	cell fu	assays	through	eleme	routin	GAS-1	of pol	invent	and ag	the in	disclo	66:1-1	Malm	216:3	et al.,	85:63	Matik	93(6):	Hentt	155(1	_
immune cells (such	as eosinophils).																													
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herein incorporated by reference in its entirety. Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) to activate or inhibit activation of immune cells include assays disclosed and/or cited in: Mayumi M., "EoL-1, a human eosinophilic cell line" Leuk Lymphoma; Jun;7(3):243-50 (1992); Bhattacharys S. "Granulocyte	macrophage colony- stimulating factor and interleukin-5 activate STAT5 and induce CIS1 mRNA in human peripheral blood eosinophils" Am J Respir Cell Mol Biol; Mar;24(3):312-6 (2001); and, Du J, et al., "Engagement of the CrkL adanter in interleukin-5	signaling in eosinophils" J Biol Chem; Oct 20;275(42):33167- 75 (2000); the contents of each of which are herein incorporated by reference in its

	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkin's lymphoma, non-Hodgkin's disease), melanoma, and prostate,
entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are a type of immune cell important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Increases in GAS mediated transcription in eosinophils is typically a result of STAT activation, normally a direct consequence of interleukin or other cytokine receptor stimulation (e.g. IL3, IL5 or GMCSF).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of
	Activation of transcription through GAS response element in immune cells (such as T-cells).
	1215
	HKACM93
	267

breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative			include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis,
cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test	GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al Gene	66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety.	Exempliary number 1 cells, such as the MOLT4 cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).
	tool the state of		

				infections associated with
				chronic oranilomatosus
			•	disease and malignant
				osteoporosis, and/or an
				infectious disease as described
				below under "Infectious
				Disease"). An additional
				preferred indication is
				idiopathic pulmonary fibrosis.
				Preferred indications include
				anemia, pancytopenia,
				leukopenia, thrombocytopenia,
				acute lymphocytic anemia
				(ALL), plasmacytomas,
				multiple myeloma, arthritis,
				AIDS, granulomatous disease,
				inflammatory bowel disease,
				sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease, and
			The state of the s	asthma and allergy.
HKACM93	1215	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include inflammation and
		through NFKB	NFKB response element are	inflammatory disorders.
		response element in	well-known in the art and may	Highly preferred indications
-		immune cells (such	be used or routinely modified	include blood disorders (e.g.,

as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below), and	immunodeficiencies (e.g., as	described below). An	additional highly preferred	indication is infection (e.g.,	AIDS, and/or an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain.
to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Gnes 15(2):105-117	(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells.
as T-cells).																						***************************************								
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			such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).	liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted
HKAEL80	1216	Activation of Natural Killer Cell ERK Signaling Pathway.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely	A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a

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method for inhibiting natural	killer cell proliferation. A	highly preferred embodiment	of the invention includes a	method for stimulating natural	killer cell differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting natural killer cell	differentiation. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), blood disorders	(e.g., as described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders			infections (e.g., as described	below under "Infectious	Disease"). Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or
modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Kyriakis JM,	Biochem Soc Symp 64:29-48	(1999); Chang and Karin,	Nature 410(6824):37-40	(2001); and Cobb MH, Prog	Biophys Mol Biol 71(3-4):479-	500 (1999); the contents of	each of which are herein	incorporated by reference in its	entirety. Natural killer cells	that may be used according to	these assays are publicly	available (e.g., through the	ATCC). Exemplary natural
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"Cardiovascular Disorders").	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include cancers such as,	kidney, melanoma, prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary cancer,	lymphoma and leukemias.	Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Other highly preferred	indications include,	pancytopenia, leukopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), arthritis, asthma,
killer cells that may be used	include the human natural	killer cell lines (for example,	NK-YT cells which have	cytolytic and cytotoxic	activity) or primary NK cells.																								
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					AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, immune
					reactions to transplanted
					organs and tissues,
					endocarditis, meningitis, Lyme
				70.00	Disease, and allergies.
1	HKAEV06	1217	Regulation of	Assays for the regulation of	A highly preferred indication
269			viability and	viability and proliferation of	is diabetes mellitus. An
-			proliferation of	cells in vitro are well-known in	additional highly preferred
			pancreatic beta	the art and may be used or	indication is a complication
			cells.	routinely modified to assess	associated with diabetes (e.g.,
				the ability of polypeptides of	diabetic retinopathy, diabetic
				the invention (including	nephropathy, kidney disease
				antibodies and agonists or	(e.g., renal failure,
				antagonists of the invention) to	nephropathy and/or other
		.,,		regulate viability and	diseases and disorders as
				proliferation of pancreatic beta	described in the "Renal
				cells. For example, the Cell	Disorders" section below),
				Titer-Glo luminescent cell	diabetic neuropathy, nerve
				viability assay measures the	disease and nerve damage
				number of viable cells in	(e.g., due to diabetic
				culture based on quantitation	neuropathy), blood vessel
				of the ATP present which	blockage, heart disease, stroke,
				signals the presence of	impotence (e.g., due to diabetic
				metabolically active cells.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
	. 100			used or routinely modified to	confusion, drowsiness,
				test regulation of viability and	nonketotic hyperglycemic-
				proliferation of pancreatic beta	hyperosmolar coma,
				cells by polypeptides of the	cardiovascular disease (e.g.,

	described in the "Cardiovascular Disorders" section below), dyslipidemia,	endocrine disorders (as described in the "Endocrine Disorders" section below), neuronathy vision impairment	(e.g., diabetic retinopathy and blindness), ulcers and impaired	wound healing, and infection (e.g., infectious diseases and	disorders as described in the "Infectious Diseases" section	below, especially of the urinary tract and skin), carpal	tunnel syndrome and Dupuytren's contracture). An	additional highly preferred indication is obesity and/or	complications associated with obesity. Additional highly	preferred indications include weight loss or alternatively.	weight gain. Additional highly	preferred indications are	insulin resistance.
invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ohtani K1 et al	Endocrinology, 139(1):172-8 (1998); Krautheim A, et al, Exp Clin Endocrinol Diabetes,	contents of each of which is herein incorporated by reference in its entirety	Pancreatic cells that may be used according to these assays	are publicly available (e.g., through the ATCC) and/or	may be routinely generated. Exemplary pancreatic cells that	may be used according to these assays include HITT15 Cells.	HITT15 are an adherent epithelial cell line established	from Syrian hamster islet cells transformed with SV40. These	cells express glucagon, somatostatin, and	glucocorticoid receptors. The cells secrete insulin, which is	stimulated by glucose and	glucagon and suppressed by somatostatin or	glucocorticoids. ATTC# CRL- insulin resistance.
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1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.			Assays for activation of	transcription are well-known in	the art and may be used and	routinely modified to assess	ability of polypeptides of the	invention to inhibit or activate	transcription. An example of	such an assay follows: Cells	were pretreated with SID	supernatants or controls for 15-	18 hours. SEAP activity was	measured after 48 hours.	LS174T is an epithelial colon	adenocarcinoma cell line. Its	tumourigenicity in nude mice	make cell line LS174T a model	for studies on the mechanism	of synthesis and secretion of	specific tumoral markers in	colon cancer. See, Patan et al.,	Circ Res, 89(8):732-39 (2001),	the contents of which are
	DT-ATP in DT-ATP-SW480	Insulin Inhibition in H4IIE	Activation of	Transcription																				
,	1217	1217	1217												*** *********************************									
	HKAEV06	HKAEV06	HKAEV06																					
	269	269		269					 1 77															

herein incorporated by reference in its entirety.	Assays for the activation of Preferred indications	transcription through the AP1 include neoplastic diseases	response element are well- (e.g., as described below under	known in the art and may be ''Hyperproliferative	used or routinely modified to Disorders"), blood disorders		polypeptides of the invention "Immune Activity",	(including antibodies and "Cardiovascular Disorders",	agonists or antagonists of the and/or "Blood-Related	invention) to modulate growth Disorders"), and infection		assays for described below under	transcription through the AP1 "Infectious Disease"). Highly	response element that may be preferred indications include	used or routinely modified to autoimmune diseases (e.g.,	test AP1-response element rheumatoid arthritis, systemic	activity of polypeptides of the lupus erythematosis, multiple	invention (including antibodies sclerosis and/or as described	and agonists or antagonists of below) and	the invention) include assays immunodeficiencies (e.g., as	disclosed in Berger et al., Gene described below). Additional	66:1-10 (1988); Cullen and highly preferred indications			et al., Proc Natl Acad Sci USA Highly preferred indications		Rellahan et al., J Biol Chem diseases (e.g., leukemia,	272(49):30806-30811 (1997); lymphoma, and/or as described	
herein incorporated by reference in its entirety	Activation of Assays for the		through AP1 response ele		lls (such	as T-cells). assess the ability of	polypeptides	including a	agonists or a	invention) to	and other cell functions.	Exemplary assays for	transcription	response ele	used or routi	test AP1-res	activity of po	invention (in	and agonists	the inventior	disclosed in	66:1-10 (198	Malm, Meth	216:362-368	et al., Proc N	85:6342-6346 (1988);	Rellahan et a	272(49):308(_
	1217																												
	HKAEV06																												_
	(569																											

				18(9):4986-4993 (1998); and	"Hyperproliferative
_				Fraser et al., Eur J Immunol	Disorders"). Highly preferred
				29(3):838-844 (1999), the	indications include neoplasms
				contents of each of which are	and cancers, such as, leukemia,
				herein incorporated by	lymphoma, prostate, breast,
-	-			reference in its entirety.	lung, colon, pancreatic,
				Human T cells that may be	esophageal, stomach, brain,
			*14	used according to these assays	liver, and urinary cancer. Other
				are publicly available (e.g.,	preferred indications include
				through the ATCC).	benign dysproliferative
				Exemplary human T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
				assays include the SUPT cell	example, hyperplasia,
-				line, which is an IL-2 and IL-4	metaplasia, and/or dysplasia.
				responsive suspension-culture	Preferred indications include
				cell line.	arthritis, asthma, AIDS,
					allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
	_				granulomatous disease,
		,			inflammatory bowel disease,
					sepsis, psoriasis, suppression of
					immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
1	HKAFK41	1218	Production of	Assays for measuring	Preferred embodiments of the
270			ICAM-1	expression of ICAM-1 are	invention include using

polypeptides of the invention	(or antibodies, agonists, or antagonists thereof) in	detection, diagnosis,	prevention, and/or treatment of	Vascular Disease,	Atherosclerosis, Restenosis,	Stroke, and Asthma.																							
>	to assess the ability of	polypeptides of the invention d	(including antibodies and p	agonists or antagonists of the	invention) to regulate ICAM-1 $\mid A$	expression. Exemplary assays S	that may be used or routinely	modified to measure ICAM-1	expression include assays	disclosed in: Rolfe BE, et al.,	Atherosclerosis, 149(1):99-110	(2000); Panettieri RA Jr, et al.,	J Immunol, 154(5):2358-2365	(1995); and, Grunstein MM, et	al., Am J Physiol Lung Cell	Mol Physiol, 278(6):L1154-	L1163 (2000), the contents of	each of which is herein	incorporated by reference in its	entirety. Cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary cells that may be	used according to these assays	include Aortic Smooth Muscle	Cells (AOSMC); such as	bovine AOSMC.
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	HKAFK41	1218	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
270				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
-				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
		na.		role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic
				(including antibodies and	lupus erythematosis, multiple
_				agonists or antagonists of the	sclerosis and/or as described
				invention) to mediate	below) and
				immunomodulation and	immunodeficiencies (e.g., as
				differentiation and modulate T	described below). Highly
				cell proliferation and function.	preferred indications also
				Exemplary assays that test for	include boosting a B cell-

	immunomodulatory proteins	mediated immune response
	 evaluate the production of	and alternatively suppressing a
	cytokines, such as IL-6, and	B cell-mediated immune
	the stimulation and	response. Highly preferred
-	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
	may be used or routinely	disorders. Additional highly
	 modified to test	preferred indications include
	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	 which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
-	Human dendritic cells that may	urinary cancer. Other preferred
	be used according to these	indications include benign
	assays may be isolated using	dysproliferative disorders and
	techniques disclosed herein or	pre-neoplastic conditions, such
	otherwise known in the art.	as, for example, hyperplasia,
	Human dendritic cells are	metaplasia, and/or dysplasia.

antagonists of the invention) to	regulate viability and	proliferation of pre-adipose	cells and cell lines. For	example, the CellTiter-Gloô	Luminescent Cell Viability	Assay (Promega Corp.,	Madison, WI, USA) can be	used to measure the number of	viable cells in culture based on	quantitation of the ATP	present which signals the	presence of metabolically	active cells. 3T3-L1 is a	mouse preadipocyte cell line. It	is a continuous substrain of	3T3 fibroblast cells developed	through clonal isolation. Cells	were differentiated to an	adipose-like state before being	used in the screen. See Green	H and Meuth M., Cell 3: 127-	133 (1974), which is herein	incorporated by reference in its	entirety.	Assays for muscle cell	ation proliferation are well known in include diabetes, myopathy,	the art and may be used or muscle cell atrophy, cancers of	SS
																									1219 Myoblast cell	proliferation		
	•																		,						HKAFT66		-/-	
																-										271		

	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel
Jun;143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain
	Insulin Secretion
	1219
	HKAFT66
	271

profeips/neptides and	blockage heart disease, stroke,
discentistion is a key	importence (e.g., due to diahetic
distribution is a ney	neuronathy or blood vessel
	incurpantly of cross reserved
Exemplary assays that may be	blockage), seizures, mental
used or routinely modified to	confusion, drowsiness,
test for stimulation of insulin	nonketotic hyperglycemic-
secretion (from pancreatic	hyperosmolar coma,
cells) by polypeptides of the	cardiovascular disease (e.g.,
invention (including antibodies	heart disease, atherosclerosis,
and agonists or antagonists of	microvascular disease,
the invention) include assays	hypertension, stroke, and other
disclosed in: Shimizu, H., et	diseases and disorders as
al., Endocr J, 47(3):261-9	described in the
(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
17 (1999); Filipsson, K., et al.,	endocrine disorders (as
Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
(1998); Olson, L.K., et al., J	Disorders" section below),
Biol Chem, 271(28):16544-52	neuropathy, vision impairment
(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
Journal of Biomolecular	blindness), ulcers and impaired
 Screening, 4:193-204 (1999),	wound healing, and infection
 the contents of each of which	(e.g., infectious diseases and
is herein incorporated by	disorders as described in the
reference in its entirety.	"Infectious Diseases" section
Pancreatic cells that may be	below, especially of the
used according to these assays	urinary tract and skin), carpal
are publicly available (e.g.,	tunnel syndrome and
through the ATCC) and/or	Dupuytren's contracture).
 may be routinely generated.	An additional highly preferred
Exemplary pancreatic cells that	indication is obesity and/or

				may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl Acad Sci. USA 78.	complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
271	HKAFT66	1219	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under

	routinely modified to assess	"Immune Activity", "Blood-
	the ability of polypeptides of	Related Disorders", and/or
	the invention (including	"Cardiovascular Disorders").
	antibodies and agonists or	Preferred indications include
	antagonists of the invention) to	autoimmune diseases (e.g.,
	regulate GATA3 transcription	rheumatoid arthritis, systemic
	factors and modulate	lupus erythematosis, multiple
	expression of mast cell genes	sclerosis and/or as described
	important for immune response	below) and
	development. Exemplary	immunodeficiencies (e.g., as
	assays for transcription	described below). Preferred
	through the GATA3 response	indications include neoplastic
	element that may be used or	diseases (e.g., leukemia,
	routinely modified to test	lymphoma, melanoma,
	GATA3-response element	prostate, breast, lung, colon,
	activity of polypeptides of the	pancreatic, esophageal,
	invention (including antibodies	stomach, brain, liver, and
	and agonists or antagonists of	urinary tract cancers and/or as
	the invention) include assays	described below under
	disclosed in Berger et al., Gene	"Hyperproliferative
	66:1-10 (1998); Cullen and	Disorders"). Other preferred
	Malm, Methods in Enzymol	indications include benign
	216:362-368 (1992); Henthorn	dysproliferative disorders and
	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
	Quant Biol 64:563-571 (1999);	Preferred indications include
	Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
	J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
-	Cell 89(4):587-596 (1997); and	acute lymphocytic anemia

				Henderson et al., Mol Cell Biol (ALL), plasmacytomas,	(ALL), plasmacytomas,
				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
- 16-				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
	**			established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
			•	many characteristics of	
				immature mast cells.	
,	HKAFT66	1219	Activation of	This reporter assay measures	Highly preferred indications
271			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
·				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under

	known in the art and may be	"Immune Activity", "Blood-
	used or routinely modified to	Related Disorders", and/or
	assess the ability of	"Cardiovascular Disorders").
	polypeptides of the invention	Preferred indications include
	(including antibodies and	autoimmune diseases (e.g.,
	agonists or antagonists of the	rheumatoid arthritis, systemic
	invention) to regulate NFAT	lupus erythematosis, multiple
	transcription factors and	sclerosis and/or as described
	modulate expression of genes	below) and
	involved in	immunodeficiencies (e.g., as
	immunomodulatory functions.	described below). Preferred
	Exemplary assays for	indications include neoplastic
	transcription through the	diseases (e.g., leukemia,
	NFAT response element that	lymphoma, melanoma,
	may be used or routinely	prostate, breast, lung, colon,
	modified to test NFAT-	pancreatic, esophageal,
	response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
	(including antibodies and	described below under
	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include
	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et al., J Immunol	leukemias, Hodgkin's disease,
	165(12):7215-7223 (2000);	acute lymphocytic anemia

				Hutchinson and McCloskey. J	(ALL), plasmacytomas.
				Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
				16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
				al., J Exp Med 188:527-537	granulomatous disease,
				(1998), the contents of each of	inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
271	HKAFT66	1219	IFNg in Human T-cell 2B9		
	HKAFT66	1219	IL-10 in Human T-		
271			cell 2B9		
	HKAFT66	1219	SEAP in Jurkat/IL4		
271			promoter		
	HKAFT66	1219	SEAP in Jurkat/IL4		
271			promoter (antiCD3		
			co-stim)	- Calaborate Control of the Control	
	HKDBF34	1220	SEAP in 293/ISRE		

			Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred	indication is infection (e.g., AIDS, and/or an infectious disease as described below under "Infectious Disease"). Highly preferred indications include neonlastic diseases
		-	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-	y of nution ad softhe
	DT-ATP in DT- ATP-SW480	SEAP in HepG2/Squale- synthetase(stimulati on)	Activation of transcription through NFKB response element in immune cells (such as T-cells).	
	1220	1220	1220	
	HKDBF34	HKDBF34	HKDBF34	
272	272	272	2726	

	99	66:1-10 (1998); Cullen and Malm Methods in Enzymol	(e.g., melanoma, leukemia, lymnhoma, and/or as described
	21.	216:362-368 (1992); Henthorn	below under
	et	et al., Proc Natl Acad Sci USA	"Hyperproliferative
	85	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	lal.	al., Virus Gnes 15(2):105-117	indications include neoplasms
	(19	(1997); and Fraser et al.,	and cancers, such as, for
	29	29(3):838-844 (1999), the	example, melanoma, renal cell
	00	contents of each of which are	carcinoma, leukemia,
	he	herein incorporated by	lymphoma, and prostate,
	ref	reference in its entirety.	breast, lung, colon, pancreatic,
	Ex	Exemplary human T cells,	esophageal, stomach, brain,
	ns	such as the MOLT4, that may	liver and urinary cancer. Other
	l pe	be used according to these	preferred indications include
	ass	assays are publicly available	benign dysproliferative
-	(e.	(e.g., through the ATCC).	disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,
		****	metaplasia, and/or dysplasia.
			Preferred indications also
			include anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
-			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
			disease, inflammatory bowel
			disease, sepsis, neutropenia,
			neutrophilia, psoriasis,
			hemophilia, hypercoagulation,

diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.			A highly preferred embodiment of the invention	includes a method for	proliferation. An alternative	highly preferred embodiment	of the invention includes a	atur			of the invention includes a	method for stimulating natural	killer cell differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting natural killer cell	differentiation. Highly	preferred indications include		described below under	"Hyperproliferative
			Kinase assay. Kinase assays, for example an Elk-1 kinase	assay, for ERK signal	proliferation or differentiation	are well known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the
	IL-8 in SW480	SEAP in ATP-3T3- L1	Activation of Natural Killer Cell	ERK Signaling	rainway.																	
	1220	1221	1221									•										
	HKDBF34	HKGAT94	HKGAT94																			
	272	273	273																			

		assavs disclosed in Forrer et	Disorders"), blood disorders
		al., Biol Chem 379(8-9):1101-	(e.g., as described below under
		1110 (1998); Kyriakis JM,	"Immune Activity",
		Biochem Soc Symp 64:29-48	"Cardiovascular Disorders",
		(1999); Chang and Karin,	and/or "Blood-Related
		Nature 410(6824):37-40	Disorders"), immune disorders
		(2001); and Cobb MH, Prog	(e.g., as described below under
		Biophys Mol Biol 71(3-4):479-	"Immune Activity") and
		500 (1999); the contents of	infections (e.g., as described
		each of which are herein	below under "Infectious
		incorporated by reference in its	Disease"). Preferred
		entirety. Natural killer cells	indications include blood
		that may be used according to	disorders (e.g., as described
		these assays are publicly	below under "Immune
		available (e.g., through the	Activity", "Blood-Related
		ATCC). Exemplary natural	Disorders", and/or
		killer cells that may be used	"Cardiovascular Disorders").
		according to these assays	Highly preferred indications
		include the human natural	include autoimmune diseases
		killer cell lines (for example,	(e.g., rheumatoid arthritis,
		NK-YT cells which have	systemic lupus erythematosis,
		cytolytic and cytotoxic	multiple sclerosis and/or as
		activity) or primary NK cells.	described below) and
			immunodeficiencies (e.g., as
			described below). Additional
			highly preferred indications
·			include inflammation and
			inflammatory disorders.
			Highly preferred indications
			also include cancers such as,
			kidney, melanoma, prostate,

breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, urinary cancer, lymphoma and leukemias. Other preferred indications include benign dysproliferative disorders and pre-neonlastic	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Other highly preferred indications include, pancytopenia, leukopenia, leukemias, Hodgkin's disease,	acute lymphocytic anemia (ALL), arthritis, asthma, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, immune reactions to transplanted organs and tissues, endocarditis, meningitis, Lyme Disease, and allergies.	A highly preferred embodiment of the invention includes a method for stimulating the production of GM-CSF. An alternative highly preferred embodiment of the invention includes a method for inhibiting the
		. LOC FEE ENGLED FO	GM-CSF FMA1. GM-CSF 18 expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytes-macrophage progenitors and enhances antimicrobial activity
			Production of GM-CSF
			1222
			HKGC027
			274

		in neutrophils, monocytes and	production of GM-CSF.
		macrophage. Additionally,	Highly preferred indications
	114	GM-CSF plays an important	include inflammation and
		role in the differentiation of	inflammatory disorders. An
		dendritic cells and monocytes,	additional highly preferred
		and increases antigen	indication is infection (e.g., as
		presentation. GM-CSF is	described below under
		considered to be a	"Infectious Disease".
		proinflammatory cytokine.	Highly preferred indications
		Assays for immunomodulatory	include blood disorders (e.g.,
		proteins that promote the	neutropenia (and the
		production of GM-CSF are	prevention of neutropenia
		well known in the art and may	(e.g., in HIV infected patients),
		be used or routinely modified	and/or as described below
		to assess the ability of	under "Immune Activity",
		polypeptides of the invention	"Blood-Related Disorders",
		(including antibodies and	and/or "Cardiovascular
		agonists or antagonists of the	Disorders"). Highly preferred
		invention) to mediate	indications also include
		immunomodulation and	autoimmune diseases (e.g.,
		modulate the growth and	rheumatoid arthritis, systemic
		differentiation of leukocytes.	lupus erythematosis, multiple
		Exemplary assays that test for	sclerosis and/or as described
		immunomodulatory proteins	below) and
		evaluate the production of	immunodeficiencies (e.g., as
		cytokines, such as GM-CSF,	described below). Additional
-12		and the activation of T cells.	highly preferred indications
		Such assays that may be used	include asthma. Highly
		or routinely modified to test	preferred indications include
		immunomodulatory activity of	neoplastic diseases (e.g.,
,		polypeptides of the invention	leukemia (e.g., acute

	(including antibodies and	lymphoblastic leukemia, and
	agonists or antagonists of the	acute myelogenous leukemia),
	invention) include the assays	lymphoma (e.g., non-
	disclosed in Miraglia et al., J	Hodgkin"s lymphoma and
	Biomolecular Screening 4:193-	
	204 (1999); Rowland et al.,	described below under
	"Lymphocytes: a practical	"Hyperproliferative
	approach" Chapter 6:138-160	Disorders"). Highly preferred
	(2000); and Ye et al., J Leukoc	indications include neoplasms
	Biol (58(2):225-233, the	and cancers, such as, leukemia,
	contents of each of which are	lymphoma, melanoma, and
	herein incorporated by	prostate, breast, lung, colon,
	reference in its entirety.	pancreatic, esophageal,
	Natural killer cells that may be	stomach, brain, liver and
	used according to these assays	urinary cancer. Other preferred
	are publicly available (e.g.,	indications include benign
	through the ATCC) or may be	dysproliferative disorders and
	isolated using techniques	pre-neoplastic conditions, such
	disclosed herein or otherwise	as, for example, hyperplasia,
	known in the art. Natural	metaplasia, and/or dysplasia.
	killer (NK) cells are large	Highly preferred indications
-	granular lymphocytes that have	include: suppression of
	cytotoxic activity but do bind	immune reactions to
	antigen. NK cells show	transplanted organs and tissues
	antibody-independent killing	(e.g., bone marrow transplant);
	of tumor cells and also	accelerating myeloid recovery;
	recognize antibody bound on	and mobilizing hematopoietic
	target cells, via NK Fc	progenitor cells. Preferred
	receptors, leading to cell-	indications include boosting a
	mediated cytotoxicity.	T cell-mediated immune
		response, and alternatively,

					suppressing a T cell-mediated immune response. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and
275	HKISB57	1223	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be	allergy. Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis

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l below)	s (e.g.,	Highly	ns also	·inhibit	eration.	ns inclu	(e.g.,	na, and/	ıder	e e	y prefer	boostin	d immu	ressing	d immu															
escribed	Tciencie	elow).	ndication	sting or	II prolife	ndicatio	diseases	ymphor	elow ur	iferative	Highl	include	mediate	ddns pu	mediate															
and/or as described below),	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting or inhibiting	immune cell proliferation	Preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative	Disorders"). Highly preferred	indications include boosting an	eosinophil-mediated immune	response, and suppressing an	eosinophil-mediated immune	response.														
	im		S								Dis	ind	eos			res				· ·				_						
ified to	eq	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the	rrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	504	(1999); Kyriakis JM, Biochem	(666);	ure	1); and	Cobb MH, Prog Biophys Mol	(1999);	f which	d by	у.	nay be	used according to these assays		tant in	ic	reactions; they are recruited to	e	inflammatory response of late		assays	utinely	•
used or routinely modified to	test JNK kinase-induced	vpeptide	iding a	r antago	the invention) include the	assays disclosed in Forrer et	379(8-	Jupta et	Cell Res 247(2): 495-504	is JM, l	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	g Biopl	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	; to thes	phils.	Eosinophils are important in	the late stage of allergic	are rec	tissues and mediate the	response	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	
routine	K kinas	of poly	on (incl	onists of	ention)	disclose	1 Chem	1998); (s 247(2	Kyriak	mp 64:2	and Kai	24):37-	IH, Pro	(3-4):4	tents of	ein inco	ce in its	lary cel.	cording	include eosinophils.	phils ar	stage o	ns; they	and me	natory 1	llergic r	ver, exe	y be us	
used or	test JN	activity	inventi	and ago	the inve	assays	al., Bio	1110 (1	Cell Re	(1999);	Soc Sy	Chang	410(68	Cobb N	Biol 71	the con	are here	referen	Exemp	used ac	include	Eosino	the late	reaction	tissues	inflamı	stage a	Moreov	that ma	
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of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999	Sep;104(3 Pt 1):565-74; and,	Sousa AR, et al., "In vivo	resistance to corticosteroids in	bronchial asthma is associated	with enhanced	phosyphorylation of JUN N-	terminal kinase and failure of	prednisolone to inhibit JUN N-
														P 414	,	(-											

				terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	
275	HKISB57	1223	Regulation of transcription of Malic Enzyme in adipocytes	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesisand its expression is stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements MEp and MEd identified as putative PPAR response elements. ME promoter may also responds to AP1 and other transcription factors. Exemplary assays that may be	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-
				used or routinely modified to test for regulation of	hyperosmolar coma, cardiovascular disease (e.g.,

	transcription of Malic Enzyme	heart disease atherosclerosis
	(in adipoocytes) by	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in: Streeper, R.S., et	section below), dyslipidemia,
	al., Mol Endocrinol,	endocrine disorders (as
	12(11):1778-91 (1998);	described in the "Endocrine
	Garcia-Jimenez, C., et al., Mol	Disorders" section below),
	Endocrinol, 8(10):1361-9	neuropathy, vision impairment
	(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
	Biol Chem, 274(25):17997-	blindness), ulcers and impaired
	8004 (1999); Ijpenberg, A., et	wound healing, and infection
	al., J Biol Chem,	(e.g., infectious diseases and
	272(32):20108-20117 (1997);	disorders as described in the
	Berger, et al., Gene 66:1-10	"Infectious Diseases" section
	(1988); and, Cullen, B., et al.,	below, especially of the
	Methods in Enzymol.	urinary tract and skin), carpal
	216:362–368 (1992), the	tunnel syndrome and
	contents of each of which is	Dupuytren's contracture).
	herein incorporated by	An additional highly preferred
	reference in its entirety.	indication is obesity and/or
	Hepatocytes that may be used	complications associated with
	according to these assays are	obesity. Additional highly
	publicly available (e.g.,	preferred indications include
	through the ATCC) and/or	weight loss or alternatively,
	may be routinely generated.	weight gain. Aditional
-	Exemplary hepatocytes that	highly preferred indications are
	may be used according to these	complications associated with
	assays includes the H4IIE rat	insulin resistance.

				liver hepatoma cell line.	
	HKMLK53	1224	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
276			Signaling Pathway	assays for signal transduction	include asthma, allergy,
	-11- 1		in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			(such as	activation, or apoptosis are	inflammation, and
_,			eosinophils).	well known in the art and may	inflammatory disorders.
				be used or routinely modified	Additional highly preferred
				to assess the ability of	indications include immune
		· · · ·		polypeptides of the invention	and hematopoietic disorders
				(including antibodies and	(e.g., as described below under
				agonists or antagonists of the	"Immune Activity", and
		***		invention) to promote or	"Blood-Related Disorders"),
				inhibit cell proliferation,	autoimmune diseases (e.g.,
				activation, and apoptosis.	rheumatoid arthritis, systemic
				Exemplary assays for JNK	lupus erythematosis, Crohn"s
				kinase activity that may be	disease, multiple sclerosis
				used or routinely modified to	and/or as described below),
				test JNK kinase-induced	immunodeficiencies (e.g., as
		73. 1		activity of polypeptides of the	described below). Highly
				invention (including antibodies	preferred indications also
				and agonists or antagonists of	include boosting or inhibiting
	-			the invention) include the	immune cell proliferation.
				assays disclosed in Forrer et	Preferred indications include
				al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
				1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
	-2010			Cell Res 247(2): 495-504	described below under
				(1999); Kyriakis JM, Biochem	"Hyperproliferative
				Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
		7-	1	Chang and Karin, Nature	indications include boosting an
				410(6824):37-40 (2001); and	eosinophil-mediated immune
				Cobb MH, Prog Biophys Mol	response, and suppressing an

eosinophil-mediated immune	response.																													,
Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are important in	the late stage of allergic	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"
	-																						-							

	Highly preferred indications include diabetes, myopathy, muscle cell atrophy, cancers of muscle (such as, rhabdomyoma, and rhabdosarcoma), cardiovascular disorders (such as congestive heart failure,
Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N- terminal kinase and failure of prednisolone to inhibit JUN N- terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Assays for muscle cell proliferation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to
	Myoblast cell proliferation
	HKMLM11 1225
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cachexia, myxomas, fibromas,	congenital cardiovascular	abnormalities, heart disease,	cardiac arrest, heart valve	disease, vascular disease, and	also as described below under	"Cardiovascular Disorders"),	stimulating myoblast	proliferation, and inhibiting	myoblast proliferation.	1																				
stimulate or inhibit myoblast	cell proliferation. Exemplary	assays for myoblast cell	proliferation that may be used	or routinely modified to test	activity of polypeptides and	antibodies of the invention	(including agonists or	antagonists of the invention)	include, for example, assays	disclosed in: Soeta, C., et al.	"Possible role for the c-ski	gene in the proliferation of	myogenic cells in regenerating	skeletal muscles of rats" Dev	Growth Differ Apr;43(2):155-	64 (2001); Ewton DZ, et al.,	"IGF binding proteins-4, -5	and -6 may play specialized	roles during L6 myoblast	proliferation and	differentiation" J Endocrinol	Mar;144(3):539-53 (1995);	and, Pampusch MS, et	al.,"Effect of transforming	growth factor beta on	proliferation of L6 and	embryonic porcine myogenic	cells" J Cell Physiol	Jun;143(3):524-8 (1990); the	contents of each of which are
																									-	,				

	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications
herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE
	Activation of transcription through serum response element in immune cells (such as T-cells).
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	HKMLP68
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the invention (including antibodies and agonists or antibodies and agonists or antibodies and agonists or antibodies and agonists or antibodies and agonists of the invention) Berger et al., Gene 66:1-10 Berger et al., Gene 66:1-10 Methods in Enzymol 216:362- 368 (1992); Henthorn et al., Methods in Enzymol 216:362- 368 (1992); Henthorn et al., Proc Natl Acad Sci USA Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by therein incorporated by the herein incorporated by the content of each of which are herein incorporated by the herein incorporated by th	or tion) in -10 n, 6:362- al., A did s s ne nae n are T T T S are c these c these c cell	or tion) in -10 n, 6:362- al., A did s s ne nae n are T T T S are c these c these c cell	or tion) in -10 n, 6:362- al., A did s s ne nae n are T T T S are c these c these c cell
the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.

esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication	is infection (e.g., an infectious	disease as described below	
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	A highly preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	growth. An alternative highly	preferred embodiment of the	invention includes a method	for inhibiting endothelial cell	growth. A highly preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	endothelial cell proliferation.	A highly preferred	embodiment of the invention	includes a method for	stimulating endothelial cell	growth. An alternative highly	preferred embodiment of the	invention includes a method	for inhibiting endothelial cell	growth. A highly preferred	+-	includes a mothod for
	Caspase Apoptosis Rescue.	Assays for caspase apoptosis	rescue are well known in the	art and may be used or	routinely modified to assess	the ability of the polypeptides	of the invention (including	antibodies and agonists or	antagonists of the invention) to	inhibit caspase protease-	mediated apoptosis.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	caspase apoptosis rescue of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Romeo et al.,	Cardiovasc Res 45(3): 788-794	(2000); Messmer et al., Br J	Pharmacol 127(7): 1633-1640	(1999); and J Atheroscler	Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety
IL-2 in Human T-cell 2B9	Protection from	Endothelial Cell	Apoptosis.																									
1226	1227																											
HKMLP68	HKMMD13																											
278	020	617																										

used according to these assays are publicly available (e.g., through commercial sources). Exemplary endothelial cells that may be used according to these assays include bovine aortic endothelial cells (bAEC), which are an example of endothelial cells which line blood vessels and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular fore, and immune cell extravasation and immune cell extravasation	lese assays endothelial cells. An		· (S				alls A highly preferred	—-	which line includes a method for	e involved stimulating angiogenisis. An		embodiment of the invention	.,.	lar tone, inhibiting angiogenesis. A	on.	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis.
	used according to the	are nublicly available	through commercial	Exemplary endothelial cells	that may be used according to	these assays include bovine	aortic endothelial cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascula	and immune cell extravasation.		-														
		-																													

cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular	disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular,	endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins	and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s

sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s
						-									***************************************			-			The second secon									

phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as	peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as	wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal	failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment

					/prevention of endometriosis
	,				and related conditions.
					Additional highly preferred
	-				indications include fibromas,
					heart disease, cardiac arrest,
					heart valve disease, and
					vascular disease. Preferred
					indications include blood
					disorders (e.g., as described
					below under "Immune
					Activity", "Blood-Related
					Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
279	HKMMD13	1227	Inhibition of squalene synthetase	Reporter Assay: construct contains regulatory and coding	

		A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention
sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.		Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or
gene transcription.	TNFa in Human T-cell 293T	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
	1228	1228
	HKMND01	HKMND01
1761	280	280

	antagonists of the invention) to	includes a method for
	promote or inhibit cell	stimulating endothelial cell
	proliferation, activation, and	proliferation. An alternative
	apoptosis. Exemplary assays	highly preferred embodiment
	for JNK and p38 kinase	of the invention includes a
	activity that may be used or	method for inhibiting
	routinely modified to test JNK	endothelial cell proliferation.
	and p38 kinase-induced	A highly preferred
	activity of polypeptides of the	embodiment of the invention
	invention (including antibodies	includes a method for
	and agonists or antagonists of	stimulating apoptosis of
	the invention) include the	endothelial cells. An
	assays disclosed in Forrer et	alternative highly preferred
	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
	are herein incorporated by	embodiment of the invention
	reference in its entirety.	includes a method for
	Endothelial cells that may be	inhibiting (e.g., decreasing) the
	used according to these assays	activation of and/or
-	are publicly available (e.g.,	inactivating endothelial cells.
	through the ATCC).	A highly preferred
	Exemplary endothelial cells	embodiment of the invention
	that may be used according to	includes a method for

	these assays include human umbilical vein endothelial cells	
	(H∪VEC), wnich are endothelial cells which line	embodiment of the invention includes a method for
	venous blood vessels, and are involved in functions that	inhibiting angiogenesis. A highly preferred embodiment
	include, but are not limited to,	of the invention includes a
	angiogenesis, vascular	method for reducing cardiac
•	permeability, vascular tone,	hypertrophy. An alternative
		of the invention includes a
		method for inducing cardiac
		hypertrophy. Highly
-		preferred indications include
		neoplastic diseases (e.g., as
		described below under
		"Hyperproliferative
		Disorders"), and disorders of
		the cardiovascular system
		(e.g., heart disease, congestive
_		heart failure, hypertension,
		aortic stenosis,
-		cardiomyopathy, valvular
		regurgitation, left ventricular
		dysfunction, atherosclerosis
		and atherosclerotic vascular
		disease, diabetic nephropathy,
-		intracardiac shunt, cardiac
		hypertrophy, myocardial
		infarction, chronic
		hemodynamic overload, and/or

		as described below under
		"Cardiovascular Disorders").
		Highly preferred indications
-		include cardiovascular,
		endothelial and/or angiogenic
		disorders (e.g., systemic
		disorders that affect vessels
		such as diabetes mellitus, as
		well as diseases of the vessels
		themselves, such as of the
		arteries, capillaries, veins
		and/or lymphatics). Highly
		preferred are indications that
		stimulate angiogenesis and/or
		cardiovascularization. Highly
		preferred are indications that
		inhibit angiogenesis and/or
		cardiovascularization.
		Highly preferred indications
		include antiangiogenic activity
		to treat solid tumors,
		leukemias, and Kaposi"s
		sarcoma, and retinal disorders.
		Highly preferred indications
		include neoplasms and cancer,
		such as, Kaposi"s sarcoma,
		hemangioma (capillary and
		cavernous), glomus tumors,
		telangiectasia, bacillary
		angiomatosis,
		hemangioendothelioma

		angiosarcoma.
		hoomong on our part
		naemangiopericytoma,
		lymphangioma,
		lymphangiosarcoma. Highly
		preferred indications also
		include cancers such as,
		prostate, breast, lung, colon,
		pancreatic, esophageal,
		stomach, brain, liver, and
		urinary cancer. Preferred
		indications include benign
		dysproliferative disorders and
		pre-neoplastic conditions, such
		as, for example, hyperplasia,
		metaplasia, and/or dysplasia.
-		Highly preferred indications
		also include arterial disease,
		such as, atherosclerosis,
		hypertension, coronary artery
		disease, inflammatory
		vasculitides, Reynaud"s
		disease and Reynaud"s
		phenomenom, aneurysms,
		restenosis; venous and
		lymphatic disorders such as
		thrombophlebitis,
		lymphangitis, and
		lymphedema; and other
		vascular disorders such as
		peripheral vascular disease,
		and cancer. Highly

preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as
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					described below under
					"Immune Activity", "Blood-
					Related Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
		-			described below). Additional
			-		preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HKMND01	1228	MCP-1 in HUVEC		
	HKMND01	1228	SEAP in OE-21		
	1111				
i	HKMND01	1228	SEAP in UMR-106		
	HL2AC08	1229	IL-2 in Human T-		
	23.0 4.0 111	0001	Cell 2931	TT (TT AT AT) 1	
	HLZAG5/	1230	Production of IL-6	IL-6 FMA1. IL-6 is produced	A highly preferred
				by T cells and has strong effects on B cells II -6	embodiment of the invention includes a method for

		participates in IL-4 induced	stimulating (e.g., increasing)
 		IgE production and increases	IL-6 production. An alternative
		IgA production (IgA plays a	highly preferred embodiment
		role in mucosal immunity).	of the invention includes a
 		IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
-		Deregulated expression of IL-6	reducing) IL-6 production. A
		has been linked to autoimmune	highly preferrred indication is
·		disease, plasmacytomas,	the stimulation or enhancement
_	,	myelomas, and chronic	of mucosal immunity. Highly
	-	hyperproliferative diseases.	preferred indications include
		Assays for immunomodulatory	blood disorders (e.g., as
	•	and differentiation factor	described below under
		proteins produced by a large	"Immune Activity", "Blood-
		variety of cells where the	Related Disorders", and/or
		expression level is strongly	"Cardiovascular Disorders"),
 <u>.</u>		regulated by cytokines, growth	and infection (e.g., as
		factors, and hormones are well	described below under
<u> </u>		known in the art and may be	"Infectious Disease"). Highly
		used or routinely modified to	preferred indications include
		assess the ability of	autoimmune diseases (e.g.,
<u>:</u>		polypeptides of the invention	rheumatoid arthritis, systemic
		(including antibodies and	lupus erythematosis, multiple
 		agonists or antagonists of the	sclerosis and/or as described
		invention) to mediate	below) and
-		immunomodulation and	immunodeficiencies (e.g., as
		differentiation and modulate T	described below). Highly
_	•	cell proliferation and function.	preferred indications also
,		Exemplary assays that test for	include boosting a B cell-
		immunomodulatory proteins	mediated immune response
 		evaluate the production of	and alternatively suppressing a
		cytokines, such as IL-6, and	B cell-mediated immune

	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
	may be used or routinely	disorders.Additional highly
	modified to test	preferred indications include
	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	 Biomolecular Screening 4:193-	"Hyperproliferative
-	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
	Human dendritic cells that may	urinary cancer. Other preferred
	be used according to these	indications include benign
	assays may be isolated using	dysproliferative disorders and
	techniques disclosed herein or	pre-neoplastic conditions, such
	otherwise known in the art.	as, for example, hyperplasia,
	Human dendritic cells are	metaplasia, and/or dysplasia.
	antigen presenting cells in	Preferred indications include
	suspension culture, which,	anemia, pancytopenia,
	when activated by antigen	leukopenia, thrombocytopenia,

				and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
283	HLCND09	1231	DT-ATP in DT-ATP-SW480		
283	HLCND09	1231	SEAP in HIB/CRE		
283	HLCND09	1231	CD152 in Human T cells		
284	HLDBE54	1232	Protection from Endothelial Cell Apoptosis.	Caspase Apoptosis Rescue. Assays for caspase apoptosis rescue are well known in the art and may be used or routinely modified to assess the ability of the polypeptides	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the

	of the invention (including	invention includes a method
	antibodies and agonists or	for inhibiting endothelial cell
	antagonists of the invention) to	growth. A highly preferred
	inhibit caspase protease-	embodiment of the invention
	mediated apoptosis.	includes a method for
	Exemplary assays for caspase	stimulating endothelial cell
	apoptosis that may be used or	proliferation. An alternative
	routinely modified to test	highly preferred embodiment
	caspase apoptosis rescue of	of the invention includes a
	polypeptides of the invention	method for inhibiting
	(including antibodies and	endothelial cell proliferation.
	agonists or antagonists of the	A highly preferred
	invention) include the assays	embodiment of the invention
	disclosed in Romeo et al.,	includes a method for
	Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
-	(2000); Messmer et al., Br J	growth. An alternative highly
	Pharmacol 127(7): 1633-1640	preferred embodiment of the
	(1999); and J Atheroscler	invention includes a method
	Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
	the contents of each of which	growth. A highly preferred
	are herein incorporated by	embodiment of the invention
	reference in its entirety.	includes a method for
	Endothelial cells that may be	stimulating apoptosis of
	used according to these assays	endothelial cells. An
	are publicly available (e.g.,	alternative highly preferred
	through commercial sources).	embodiment of the invention
	Exemplary endothelial cells	includes a method for
	that may be used according to	inhibiting (e.g., decreasing)
	these assays include bovine	apoptosis of endothelial cells.
	aortic endothelial cells	A highly preferred
	(bAEC), which are an example	embodiment of the invention

includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial
of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.																							

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hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi's sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,
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								-																						
				_																										

hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease.
10 10 10 10 10 10 10 10																														

and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury	such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring,	ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal	diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke	graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders.	age-related macular degeneration, and treatment /prevention of endometriosis	Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood
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disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.		eins embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An exert a alternative highly preferred embodiment of the invention
		TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory
	Caspase (+paclitaxel) in SW480	Production of TNF alpha by dendritic cells
	1232	1233
	HLDBE54	HLDBX13
	284	285

includes a method for	stimulating (e.g., increasing)	TNF alpha production.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn's disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma.
and cytotoxic effects on a	variety of cells are well known	in the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	modulate inflammation and	cytotoxicity. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or	cytotoxic response. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160
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																			-			٠								

and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted
(2000); Verhasselt et al., Eur J	Immunol 28(11):3886-3890	(1198); Dahlen et al., J	Immunol 160(7):3585-3593	(1998); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.								
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		_																												
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organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for
	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of
	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
	1233
	HLDBX13
	285

	the invention) include the	endothelial cells. An
	 assays disclosed in Forrer et	alternative highly preferred
	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	 (1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
-	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
	 are herein incorporated by	embodiment of the invention
	 reference in its entirety.	includes a method for
	 Endothelial cells that may be	inhibiting (e.g., decreasing) the
	used according to these assays	activation of and/or
	are publicly available (e.g.,	inactivating endothelial cells.
	through the ATCC).	A highly preferred
	 Exemplary endothelial cells	embodiment of the invention
	that may be used according to	includes a method for
	these assays include human	stimulating angiogenisis. An
	umbilical vein endothelial cells	alternative highly preferred
	(HUVEC), which are	embodiment of the invention
	endothelial cells which line	includes a method for
	 venous blood vessels, and are	inhibiting angiogenesis. A
	 involved in functions that	highly preferred embodiment
	 include, but are not limited to,	of the invention includes a
	 angiogenesis, vascular	method for reducing cardiac
	 permeability, vascular tone,	hypertrophy. An alternative
	 and immune cell extravasation.	highly preferred embodiment
		of the invention includes a

		mothod for inducing condice
		יווכנווטם וטו וווטמכוווצ כמומומכ
		nypertrophy. Highly
		preferred indications include
	,	neoplastic diseases (e.g., as
		described below under
		"Hyperproliferative
		Disorders"), and disorders of
		the cardiovascular system
		(e.g., heart disease, congestive
		heart failure, hypertension,
		aortic stenosis,
		cardiomyopathy, valvular
		regurgitation, left ventricular
		dysfunction, atherosclerosis
		and atherosclerotic vascular
		disease, diabetic nephropathy,
		intracardiac shunt, cardiac
		hypertrophy, myocardial
		infarction, chronic
		hemodynamic overload, and/or
		as described below under
		"Cardiovascular Disorders").
		Highly preferred indications
,		include cardiovascular,
		endothelial and/or angiogenic
		disorders (e.g., systemic
		disorders that affect vessels
		such as diabetes mellitus, as
		well as diseases of the vessels
		themselves, such as of the
		arteries, capillaries, veins

and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that	inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors,	sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors,	telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also	include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign
			<u>.</u>	

					dysproliferative disorders and	P
					nre-neonlastic conditions such	do.
		-			pre-incopiastic conditions, su	
		_			as, for example, hyperplasia,	<u>-</u> -
_		-			metaplasia, and/or dysplasia.	
		-			Highly preferred indications	
					also include arterial disease,	
-	•	-			such as, atherosclerosis,	
-					hypertension, coronary artery	-Ty
	_	<u>-</u>			disease, inflammatory	
					vasculitides, Reynaud"s	
					disease and Reynaud"s	_
					phenomenom, aneurysms,	
		 -			restenosis; venous and	
					lymphatic disorders such as	
					thrombophlebitis,	
					lymphangitis, and	
					lymphedema; and other	
					vascular disorders such as	
		- ·			peripheral vascular disease,	
					and cancer. Highly	
					preferred indications also	
					include trauma such as	
					wounds, burns, and injured	
					tissue (e.g., vascular injury	
	-				such as, injury resulting from	u u
					balloon angioplasty, and	
_					atheroschlerotic lesions),	
	_	-			implant fixation, scarring,	
					ischemia reperfusion injury,	
					rheumatoid arthritis,	
				1	cerebrovascular disease, renal	lal

failure and osteonorosis	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and

described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.		A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method
		Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies
	VEGF in SW480	Activation of Adipocyte ERK Signaling Pathway
	1233	1234
	HLDBX13	HLDNA86
	285	286

	8	and agonists or antagonists of	for atimisoting (
		ra agometa or antagometa or	ioi sumuating (e.g.,
	oun —	the invention) include the	increasing) adipocyte
	as	assays disclosed in Forrer et	activation. An alternative
	al	al., Biol Chem 379(8-9):1101-	highly preferred embodiment
	11	1110 (1998); Le Marchand-	of the invention includes a
	Br	Brustel Y, Exp Clin	method for inhibiting the
		Endocrinol Diabetes	activation of (e.g., decreasing)
	10	107(2):126-132 (1999);	and/or inactivating adipocytes.
		Kyriakis JM, Biochem Soc	Highly preferred indications
	Sy	Symp 64:29-48 (1999); Chang	include endocrine disorders
	an	and Karin, Nature	(e.g., as described below under
·	41	410(6824):37-40 (2001); and	"Endocrine Disorders").
	<u> </u>	Cobb MH, Prog Biophys Mol	Highly preferred indications
	Bi	Biol 71(3-4):479-500 (1999);	also include neoplastic
	the	the contents of each of which	diseases (e.g., lipomas,
	are	are herein incorporated by	liposarcomas, and/or as
	ref	reference in its entirety.	described below under
	W	Mouse adipocyte cells that	"Hyperproliferative
	em	may be used according to these	Disorders"). Preferred
	ass	assays are publicly available	indications include blood
	(e.	(e.g., through the ATCC).	disorders (e.g., hypertension,
	Ex	Exemplary mouse adipocyte	congestive heart failure, blood
	eel	cells that may be used	vessel blockage, heart disease,
		according to these assays	stroke, impotence and/or as
	inc	include 3T3-L1 cells. 3T3-L1	described below under
	is	is an adherent mouse	"Immune Activity",
	pre	preadipocyte cell line that is a	"Cardiovascular Disorders",
	001	continuous substrain of 3T3	and/or "Blood-Related
	fib	fibroblast cells developed	Disorders"), immune disorders
	thr	through clonal isolation and	(e.g., as described below under
)un	undergo a pre-adipocyte to	"Immune Activity"), neural

disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), and infection (e.g., as described below under	"Infectious Disease"). A highly preferred indication is diabetes mellitus.	additional highly preferred indication is a complication	diabetic retinopathy, diabetic nephropathy, kidney disease	(e.g., renal failure, nephropathy and/or other	diseases and disorders as described in the "Renal	Disorders" section below), diabetic neuronathy, nerve	disease and nerve damage	neuropathy), blood vessel	blockage, heart disease, stroke, impotence (e.g., due to diabetic	neuropathy or blood vessel blockage), seizures, mental	confusion, drowsiness,	hyperosmolar coma,	cardiovascular disease (e.g.,
adipose-like conversion under appropriate differentiation conditions known in the art.													
								•			•		
													

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	י י י י י י י י י י י י י י י י י י י	stast,
-	hypertension, stroke, and other	oke, and other
	diseases and disorders as	rders as
	described in the	
	"Cardiovascular Disorders"	Disorders"
	section below), dyslipidemia,	yslipidemia,
	endocrine disorders (as	ers (as
	described in the "Endocrine	Endocrine
	Disorders" section below),	n below),
	neuropathy, vision impairment	n impairment
	(e.g., diabetic retinopathy and	inopathy and
	blindness), ulcers and impaired	and impaired
	wound healing, infection (e.g.,	nfection (e.g.,
	infectious diseases and	ss and
	disorders as described in the	ribed in the
	"Infectious Diseases" section	ses" section
	below (particularly of the	ly of the
	urinary tract and skin).	skin). An
	additional highly preferred	preferred
	indication is obesity and/or	ity and/or
	complications associated with	sociated with
	obesity. Additional highly	nal highly
	preferred indications include	ons include
	weight loss or alternatively,	ernatively,
	weight gain.	Additional
	highly preferred indications are	indications are
	complications associated with	sociated with
	insulin resistance.	··
	Additional highly preferred	preferred
	indications are disorders of the	sorders of the
	musculoskeletal systems	systems

					including myopathies,
					muscular dystropny, and/or as described herein.
					Additional highly preferred
					indications include,
					hypertension, coronary artery
					disease, dyslipidemia,
					gallstones, osteoarthritis,
					degenerative arthritis, eating
					disorders, fibrosis, cachexia,
					and kidney diseases or
					disorders. Preferred
					indications include neoplasms
					and cancer, such as,
					lymphoma, leukemia and
					breast, colon, and kidney
					cancer. Additional preferred
		_	*		indications include melanoma,
					prostate, lung, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer.
					Highly preferred indications
					include lipomas and
			7.		liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
HLDON23	N23	1235	Regulation of	Assays for the regulation of	A highly preferred indication is diabetes mellitus
			uanscripnon	nanscription though the	maication is diabetes menus.

		through the PEPCK	PEPCK promoter are well-	An additional highly preferred
		promoter in	known in the art and may be	indication is a complication
		hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
	7/81-		assess the ability of	diabetic retinopathy, diabetic
			polypeptides of the invention	nephropathy, kidney disease
			(including antibodies and	(e.g., renal failure,
			agonists or antagonists of the	nephropathy and/or other
			invention) to activate the	diseases and disorders as
			PEPCK promoter in a reporter	described in the "Renal
			construct and regulate liver	Disorders" section below),
			gluconeogenesis. Exemplary	diabetic neuropathy, nerve
		•	assays for regulation of	disease and nerve damage
			transcription through the	(e.g., due to diabetic
			PEPCK promoter that may be	neuropathy), blood vessel
			used or routinely modified to	blockage, heart disease, stroke,
1.7			test for PEPCK promoter	impotence (e.g., due to diabetic
			activity (in hepatocytes) of	neuropathy or blood vessel
			polypeptides of the invention	blockage), seizures, mental
			(including antibodies and	confusion, drowsiness,
			agonists or antagonists of the	nonketotic hyperglycemic-
			invention) include assays	hyperosmolar coma,
		7	disclosed in Berger et al., Gene	cardiovascular disease (e.g.,
			66:1-10 (1998); Cullen and	heart disease, atherosclerosis,
			Malm, Methods in Enzymol	microvascular disease,
			216:362-368 (1992); Henthorn	hypertension, stroke, and other
			et al., Proc Natl Acad Sci USA	diseases and disorders as
	~~		85:6342-6346 (1988);	described in the
			Lochhead et al., Diabetes	"Cardiovascular Disorders"
			49(6):896-903 (2000); and	section below), dyslipidemia,
			Yeagley et al., J Biol Chem	endocrine disorders (as
			275(23):17814-17820 (2000),	described in the "Endocrine

Disorders" section below),	(e a dispetic retinonathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	an infectious diseases or	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include glycogen	storage disease (e.g.,
the contents of each of which is herein incorporated by	reference in its entirety	Hepatocyte cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary liver hepatoma	cells that may be used	according to these assays	include H4lle cells, which	contain a tyrosine amino	transferase that is inducible	with glucocorticoids, insulin,	or cAMP derivatives.															
		1.0																		-									
		-									-	-			-					1816									

glycogenoses), hepatitis,	gallstones, cirrhosis of the	liver, degenerative or necrotic	liver disease, alcoholic liver	diseases, fibrosis, liver	regeneration, metabolic	disease, dyslipidemia and	cholesterol metabolism, and	hepatocarcinomas.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), infection	(e.g., an infectious disease	and/or disorder as described	below under "Infectious	Disease"), endocrine disorders	(e.g., as described below under	"Endocrine Disorders"), and	neural disorders (e.g., as	described below under "Neural	Activity and Neurological	Diseases").	Additional preferred	indications include neoplastic	diseases (e.g., as described
		_										-																		
						-		,,,								-														

1235 Production of IL-10 and activation of T-cells.	agonists or antagonists of the invention) to regulate ICAM-1 Disease, Athereosclerosis, expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays	disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733- 1739 (2000), the contents of each of which is herein	entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Assays for production of IL-10 Highly preferred indications and activation of T-cells are well known in the art and may be used or routinely modified indications include immune to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention and polypeptides of the invention (including antibodies and "Immune Activity", and "Immune
	agonists inventior expressic that may modified expressic	disclosed FASEB J (2001); a al., Am J 1739 (20 each of w	entirety. used according are public through the properties of the	ctivation of IL-10
i limitati di manana				HLDON23 1235

-			
		inhibit production of IL-10	rheumatoid arthritis, systemic
_		and/or activation of T-cells.	lupus erythematosis, Crohn"s
		Exemplary assays that may be	disease, multiple sclerosis
		used or routinely modified to	and/or as described below),
		assess the ability of	immunodeficiencies (e.g., as
-		polypeptides and antibodies of	described below), boosting a T
		the invention (including	cell-mediated immune
		agonists or antagonists of the	response, and suppressing a T
		invention) to modulate IL-10	cell-mediated immune
		production and/or T-cell	response.
		proliferation include, for	
		example, assays such as	
		disclosed and/or cited in:	
	•	Robinson, DS, et al., "Th-2	
		cytokines in allergic disease"	
		Br Med Bull; 56 (4): 956-968	
		(2000), and Cohn, et al., "T-	
_		helper type 2 cell-directed	
		therapy for asthma"	
		Pharmacology & Therapeutics;	
		88: 187-196 (2000); the	
_		contents of each of which are	
		herein incorporated by	
		reference in their entirety.	
	-	Exemplary cells that may be	
		used according to these assays	
		include Th2 cells. IL10	
		secreted from Th2 cells may be	
		measured as a marker of Th2	
		cell activation. Th2 cells are	
	· · · · · · · · · · · · · · · · · · ·	a class of T cells that secrete	

		Highly preferred indications	include allergy, asthma, and	rhinitis. Additional preferred		(e.g., an infectious disease as	described below under	"Infectious Disease"), and	inflammation and	inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,
IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.		This reporter assay measures	activation of the GATA-3	signaling pathway in HMC-1	human mast cell line.	Activation of GATA-3 in mast	cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription	through the GATA3 response	element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to
	SEAP in HIB/CRE	Activation of	transcription	through GATA-3	response element in	immune cells (such	as mast cells).	_										
	1236	1236																
	HLDOW79	HLDOW79																
	288		288									-						

																													_
rheumatoid arthritis, systemic lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowyel disease
regulate GATA3 transcription factors and modulate	expression of mast cell genes	important for immune response	development. Exemplary	assays for transcription	through the GATA3 response	element that may be used or	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast
		-													-										-				
							-																-						
																								776					

sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g.,
cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and
	Activation of transcription through NFAT response element in immune cells (such as mast cells).
	1236
	HLDOW79
	288

	agonists or antagonists of the	rheumatoid arthritis, systemic
	invention) to regulate NFAT	lupus erythematosis, multiple
	transcription factors and	sclerosis and/or as described
	modulate expression of genes	below) and
	involved in	immunodeficiencies (e.g., as
	immunomodulatory functions.	described below). Preferred
 	 Exemplary assays for	indications include neoplastic
	 transcription through the	diseases (e.g., leukemia,
	 NFAT response element that	lymphoma, melanoma,
-	may be used or routinely	prostate, breast, lung, colon,
	modified to test NFAT-	pancreatic, esophageal,
	 response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
	 (including antibodies and	described below under
_	agonists or antagonists of the	"Hyperproliferative
	 invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	 216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	 et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	 85:6342-6346 (1988); De Boer	Preferred indications include
	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et al., J Immunol	leukemias, Hodgkin's disease,
	 165(12):7215-7223 (2000);	acute lymphocytic anemia
	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
	 16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
	al., J Exp Med 188:527-537	granulomatous disease,
	(1998), the contents of each of	inflammatory bowel disease,

sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	
which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1236
	HLDOW79
	288

				Assay (Promega Corp., Madison, WI. USA) can be	
	71			used to measure the number of	
				quantitation of the ATP	
				present which signals the	
				presence of metabolically	
				active cells. 3T3-L1 is a	
				mouse preadipocyte cell line. It	
				1s a continuous substrain of	
				3T3 fibroblast cells developed	
				through clonal isolation. Cells	
				were differentiated to an	
				adipose-like state before being	
			-	used in the screen. See Green	,
				H and Meuth M., Cell 3: 127-	
				133 (1974), which is herein	
		-424		incorporated by reference in its	
				entirety.	
	HLDOW79	1236	SEAP in Jurkat/IL4		
288			promoter		
	HLDOW79	1236	SEAP in Jurkat/IL4		
288			promoter (antiCD3		
			co-stim)		
6	HLDOW79	1236	Activation of	Assays for the activation of	Preferred indications
288			transcription	transcription through the AP1	include neoplastic diseases
			through AP1	response element are well-	(e.g., as described below under
			response element in	known in the art and may be	"Hyperproliferative
			immune cells (such	used or routinely modified to	Disorders"), blood disorders
			as T-cells).	assess the ability of	(e.g., as described below under
				polypeptides of the invention	"Immune Activity".

	(i)	(including antibodies and	"Cardiovascular Disorders".
	38	agonists or antagonists of the	and/or "Blood-Related
	. u	invention) to modulate growth	Disorders"), and infection
	ar	and other cell functions.	(e.g., an infectious disease as
	<u> </u>	Exemplary assays for	described below under
	<u> </u>	transcription through the AP1	"Infectious Disease"). Highly
	re	response element that may be	preferred indications include
	sn	used or routinely modified to	autoimmune diseases (e.g.,
	te	test AP1-response element	rheumatoid arthritis, systemic
	<u>ac</u>	activity of polypeptides of the	lupus erythematosis, multiple
	ni	invention (including antibodies	sclerosis and/or as described
	ar	and agonists or antagonists of	below) and
		the invention) include assays	immunodeficiencies (e.g., as
	<u>di</u>	disclosed in Berger et al., Gene	described below). Additional
)9	66:1-10 (1988); Cullen and	highly preferred indications
	<u> </u>	Malm, Methods in Enzymol	include inflammation and
		216:362-368 (1992); Henthorn	inflammatory disorders.
	et	et al., Proc Natl Acad Sci USA	Highly preferred indications
	5 8	85:6342-6346 (1988);	also include neoplastic
		Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	27	272(49):30806-30811 (1997);	lymphoma, and/or as described
		Chang et al., Mol Cell Biol	below under
-	- 18	18(9):4986-4993 (1998); and	"Hyperproliferative
	<u>H</u>	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29	29(3):838-844 (1999), the	indications include neoplasms
	3	contents of each of which are	and cancers, such as, leukemia,
	he	herein incorporated by	lymphoma, prostate, breast,
	Fe	reference in its entirety.	lung, colon, pancreatic,
	H	Human T cells that may be	esophageal, stomach, brain,
-	sn en	used according to these assays	liver, and urinary cancer. Other
	ar	are publicly available (e.g.,	preferred indications include

				through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is an IL-2 and IL-4 responsive suspension-culture cell line.	benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL),
					plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
288	HLDOW79	1236	Activation of transcription through CD28 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells.	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for

Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Exemplary assays for transcription through the C response element that may used or routinely modified test CD28-response elemen activity of polypeptides of invention (including antibo and agonists or antagonists the invention) include assa disclosed in Berger et al., 66:1-10 (1998); Cullen and Malm, Methods in Enzym 216:362-368 (1992); Hentl et al., Proc Natl Acad Sci 185:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-132 (1997); Parra et al., J Imm 166(4):2437-2443 (2001); Butscher et al., J Biol Che 3(1):552-560 (1998), the contents of each of which herein incorporated by reference in its entirety. T cells that may be used according to these assays publicly available (e.g., through the ATCC).	Exemplary assays for transcription through the C response element that may used or routinely modified test CD28-response elemen activity of polypeptides of invention (including antibo and agonists or antagonists the invention) include assa disclosed in Berger et al., 66:1-10 (1998); Cullen and Malm, Methods in Enzym 216:362-368 (1992); Henti et al., Proc Natl Acad Sci 185:6342-6346 (1988); McGuire and Lacobelli, J Immunol 159(3):1319-132 (1997); parra et al., J Imm 166(4):2437-2443 (2001); Butscher et al., J Biol Che 3(1):552-560 (1998), the contents of each of which herein incorporated by reference in its entirety. Tells that may be used according to these assays a publicly available (e.g., through the ATCC).	\vdash	<u>~</u>	be embodiment of the invention		nt inhibiting the activation of				ys includes a method for	Gene stimulating (e.g., increasing)		ol highly preferred embodiment	Ш		reducing) IL-2 production.	Additional highly preferred	7 indications include	unol inflammation and	and inflammatory disorders.			-	systemic lupus erythematosis,	multiple sclerosis and/or as	described below),		described below), boosting a T		that response, and suppressing a T	
			Exemplary assays for	transcription through the C	response element that may	used or routinely modified	test CD28-response elemer	activity of polypeptides of	invention (including antibo	and agonists or antagonists	the invention) include assa	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzyme	216:362-368 (1992); Hentl	et al., Proc Natl Acad Sci I	85:6342-6346 (1988);	McGuire and Iacobelli, J	Immunol 159(3):1319-132	(1997); Parra et al., J Imm	166(4):2437-2443 (2001); and	Butscher et al., J Biol Cher	3(1):552-560 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays a	publicly available (e.g.,	through the ATCC).	Exemplary human T cells	

		line, which is a suspension	indications include fleoplastic
		culture of IL-2 and IL-4	diseases (e.g., melanoma, renal
	 	responsive T cells.	cell carcinoma, leukemia,
			lymphoma, and/or as described
			below under
	1.72		"Hyperproliferative
			Disorders"). Highly preferred
			indications include neoplasms
			and cancers, such as, for
			example, melanoma (e.g.,
			metastatic melanoma), renal
_			cell carcinoma (e.g., metastatic
			renal cell carcinoma),
			leukemia, lymphoma (e.g., T
			cell lymphoma), and prostate,
			breast, lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
			A highly preferred indication
			includes infection (e.g.,
			AIDS, tuberculosis, infections
	 		associated with granulomatous
			disease, and osteoporosis,
			and/or as described below

					highly preferred indication is
					AIDS. Additional highly
					preferred indications include
					suppression of immune
• • • • • • • • • • • • • • • • • • • •					reactions to transplanted
					organs and/or tissues, uveitis,
					psoriasis, and tropical spastic
			. 1/1		paraparesis. Preferred
					indications include blood
		***			disorders (e.g., as described
					below under "Immune
					Activity", "Blood-Related
					Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications also
					include anemia, pancytopenia,
•••	1 - 11				leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
		-			meningitis, Lyme Disease,
					asthma and allergy.
0	HLDOW79	1236	Activation of	Assays for the activation of	Highly preferred indications
887			transcription	transcription through the	include blood disorders (e.g.,

	through NFAT	Nuclear Factor of Activated T	as described below under
	response element in	cells (NFAT) response element	"Immune Activity", "Blood-
	immune cells (such	are well-known in the art and	Related Disorders", and/or
	as T-cells).	may be used or routinely	"Cardiovascular Disorders").
		modified to assess the ability	Highly preferred indications
		of polypeptides of the	include autoimmune diseases
		invention (including antibodies	(e.g., rheumatoid arthritis,
		and agonists or antagonists of	systemic lupus erythematosis,
		the invention) to regulate	multiple sclerosis and/or as
		NFAT transcription factors and	described below),
		modulate expression of genes	immunodeficiencies (e.g., as
	-	involved in	described below), boosting a T
		immunomodulatory functions.	cell-mediated immune
		Exemplary assays for	response, and suppressing a T
		transcription through the	cell-mediated immune
		NFAT response element that	response. Additional highly
		may be used or routinely	preferred indications include
		modified to test NFAT-	inflammation and
		response element activity of	inflammatory disorders. An
		polypeptides of the invention	additional highly preferred
		(including antibodies and	indication is infection (e.g., an
		agonists or antagonists of the	infectious disease as described
		invention) include assays	below under "Infectious
		disclosed in Berger et al., Gene	Disease"). Preferred
		66:1-10 (1998); Cullen and	indications include neoplastic
-		Malm, Methods in Enzymol	diseases (e.g., leukemia,
		216:362-368 (1992); Henthorn	lymphoma, and/or as described
		et al., Proc Natl Acad Sci USA	below under
		85:6342-6346 (1988); Serfling	"Hyperproliferative
-		et al., Biochim Biophys Acta	Disorders"). Preferred
		1498(1):1-18 (2000); De Boer	indications include neoplasms

				et al., Int J Biochem Cell Biol	and cancers, such as, for
		~.		31(10):1221-1236 (1999);	example, leukemia, lymphoma,
				Fraser et al., Eur J Immunol	and prostate, breast, lung,
				29(3):838-844 (1999); and	colon, pancreatic, esophageal,
				Yeseen et al., J Biol Chem	stomach, brain, liver and
	-			268(19):14285-14293 (1993),	urinary cancer. Other preferred
				the contents of each of which	indications include benign
				are herein incorporated by	dysproliferative disorders and
	-			reference in its entirety. T	pre-neoplastic conditions, such
				cells that may be used	as, for example, hyperplasia,
				according to these assays are	metaplasia, and/or dysplasia.
-				publicly available (e.g.,	Preferred indications also
				through the ATCC).	include anemia, pancytopenia,
				Exemplary human T cells that	leukopenia, thrombocytopenia,
				may be used according to these	Hodgkin's disease, acute
, -				assays include the SUPT cell	lymphocytic anemia (ALL),
				line, which is a suspension	plasmacytomas, multiple
				culture of IL-2 and IL-4	myeloma, Burkitt's lymphoma,
				responsive T cells.	arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
-					neutrophilia, psoriasis,
			-		suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
	- -				diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
288	HLDOW79	1236	Activation of transcription	Assays for the activation of transcription through the	Highly preferred indications include inflammation and

	through NFKB	NFKB response element are	inflammatory disorders.
	response element in	well-known in the art and may	Highly preferred indications
 	immune cells (such	be used or routinely modified	include blood disorders (e.g.,
	as T-cells).	to assess the ability of	as described below under
 		polypeptides of the invention	"Immune Activity", "Blood-
		(including antibodies and	Related Disorders", and/or
 		agonists or antagonists of the	"Cardiovascular Disorders").
		invention) to regulate NFKB	Highly preferred indications
 		transcription factors and	include autoimmune diseases
		modulate expression of	(e.g., rheumatoid arthritis,
 		immunomodulatory genes.	systemic lupus erythematosis,
		Exemplary assays for	multiple sclerosis and/or as
_		transcription through the	described below), and
		NFKB response element that	immunodeficiencies (e.g., as
 		may be used or rountinely	described below). An
 		modified to test NFKB-	additional highly preferred
		response element activity of	indication is infection (e.g.,
 		polypeptides of the invention	AIDS, and/or an infectious
		(including antibodies and	disease as described below
		agonists or antagonists of the	under "Infectious Disease").
		invention) include assays	Highly preferred indications
 		disclosed in Berger et al., Gene	include neoplastic diseases
 	-	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
 		Malm, Methods in Enzymol	lymphoma, and/or as described
		216:362-368 (1992); Henthorn	below under
 		et al., Proc Natl Acad Sci USA	"Hyperproliferative
		85:6342-6346 (1988); Black et	Disorders"). Highly preferred
		al., Virus Gnes 15(2):105-117	indications include neoplasms
 		(1997); and Fraser et al.,	and cancers, such
		29(3):838-844 (1999), the	as,melanoma, renal cell
		contents of each of which are	carcinoma, leukemia,

				herein incorporated by	lymphoma, and prostate,
				reference in its entirety. T	breast, lung, colon, pancreatic,
				cells that may be used	esophageal, stomach, brain,
				according to these assays are	liver and urinary cancer. Other
				publicly available (e.g.,	preferred indications include
				through the ATCC).	benign dysproliferative
				Exemplary human T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
				assays include the SUPT cell	example, hyperplasia,
	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,			line, which is a suspension	metaplasia, and/or dysplasia.
	_			culture of IL-2 and IL-4	Preferred indications also
				responsive T cells.	include anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
·					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
	HLDQC46	1237	Activation of	Assays for the activation of	A preferred embodiment of
289			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,

																										-				
reducing) TNF alpha	production. An alternative	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) TNF alpha	production. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis An additional highly
(SRE) are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate the serum response	factors and modulate the	expression of genes involved	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used
response element in	immune cells (such	as T-cells).						-										-												

																				,		-								

	according to these assays are	nreferred indication is sensis
	miblicly available (a g	Lighty anofomed indications
	puoliciy available (c.g.,	riginiy preferred indications
	through the A1CC).	include neoplastic diseases
	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
	may be used according to these	and/or as described below
	assays include the CTLL cell	under "Hyperproliferative
	line, which is an IL-2	Disorders"). Additionally,
-	dependent suspension culture	highly preferred indications
	of T cells with cytotoxic	include neoplasms and
 	activity.	cancers, such as, for example,
		leukemia, lymphoma,
		melanoma, glioma (e.g.,
	•	malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
		anemia, pancytopenia,
		leukopenia, thrombocytopenia,
 		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
3000		arthritis, AIDS, granulomatous

disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred indication is diabetes mellitus. An additional highly preferred indication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel
	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation
	Regulation of viability and proliferation of pancreatic beta cells.
	1238
	HLDQR62
·	290

		of the ATP present which	blockage, heart disease, stroke,
		signals the presence of	impotence (e.g., due to diabetic
		metabolically active cells.	neuropathy or blood vessel
 		Exemplary assays that may be	blockage), seizures, mental
		used or routinely modified to	confusion, drowsiness,
 .=		test regulation of viability and	nonketotic hyperglycemic-
 -		proliferation of pancreatic beta	hyperosmolar coma,
 -		cells by polypeptides of the	cardiovascular disease (e.g.,
 		invention (including antibodies	heart disease, atherosclerosis,
		and agonists or antagonists of	microvascular disease,
 . •		the invention) include assays	hypertension, stroke, and other
 		disclosed in: Friedrichsen BN,	diseases and disorders as
		et al., Mol Endocrinol,	described in the
 		15(1):136-48 (2001); Huotari	"Cardiovascular Disorders"
 _		MA, et al., Endocrinology,	section below), dyslipidemia,
 		139(4):1494-9 (1998); Hugl	endocrine disorders (as
 		SR, et al., J Biol Chem 1998	described in the "Endocrine
 		Jul 10;273(28):17771-9	Disorders" section below),
 		(1998), the contents of each of	neuropathy, vision impairment
		which is herein incorporated	(e.g., diabetic retinopathy and
 		by reference in its entirety.	blindness), ulcers and impaired
		Pancreatic cells that may be	wound healing, and infection
		used according to these assays	(e.g., infectious diseases and
 		are publicly available (e.g.,	disorders as described in the
 		through the ATCC) and/or	"Infectious Diseases" section
 		may be routinely generated.	below, especially of the
		Exemplary pancreatic cells that	urinary tract and skin), carpal
 		may be used according to these	tunnel syndrome and
 		assays include rat INS-1 cells.	Dupuytren's contracture). An
		INS-1 cells are a semi-	additional highly preferred
		adherent cell line established	indication is obesity and/or

				from cells isolated from an X-ray induced rat transplantable	complications associated with obesity. Additional highly
				insulinoma. These cells retain characteristics typical of native	preferred indications include weight loss or alternatively,
				pancreatic beta cells including	weight gain. Additional highly
				glucose inducible insulin	preferred indications are
				secretion. References: Asfari	complications associated with
				et al. Endocrinology 1992	insulin resistance.
				130:16/.	
,	HLDQR62	1238	Activation of	Assays for the activation of	Preferred indications include
290			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
	,		response element in	well-known in the art and may	"Immune Activity", "Blood-
			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
				(including antibodies and	infectious disease as described
				agonists or antagonists of the	below under "Infectious
				invention) to increase cAMP	Disease"). Preferred
				and regulate CREB	indications include
				transcription factors, and	autoimmune diseases (e.g.,
				modulate expression of genes	rheumatoid arthritis, systemic
				involved in a wide variety of	lupus erythematosis, multiple
				cell functions. Exemplary	sclerosis and/or as described
				assays for transcription	below), immunodeficiencies
				through the cAMP response	(e.g., as described below),
				element that may be used or	boosting a T cell-mediated
				routinely modified to test	immune response, and
				cAMP-response element	suppressing a T cell-mediated
	-			activity of polypeptides of the	immune response. Additional
				invention (including antibodies	preferred indications include

													_														
inflammation and inflammatory disorders.		include neoplastic diseases (e.g., leukemia, lymphoma	and/or as described below	under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma	(e.g., T cell lymphoma,	Burkitt's lymphoma, non-	Hodgkins lymphoma,	Hodgkin"s disease),	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,
and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Genes 15(2):105-117	(1997); and Belkowski et al., J	Immunol 161(2):659-665	(1998), the contents of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is a suspension	culture of IL-2 dependent	cytotoxic T cells.				-		
				•										-													
										-			•						•		<u>.</u>						
															_					-				341	-		

					AIDS, granulomatous disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
		pa.			organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
	НГДОП 19	1239	Regulation of	Assays for the regulation of	A highly preferred indication
			viability and	viability and proliferation of	is diabetes mellitus. An
			proliferation of	cells in vitro are well-known in	additional highly preferred
			pancreatic beta	the art and may be used or	indication is a complication
			cells.	routinely modified to assess	associated with diabetes (e.g.,
				the ability of polypeptides of	diabetic retinopathy, diabetic
				the invention (including	nephropathy, kidney disease
				antibodies and agonists or	(e.g., renal failure,
				antagonists of the invention) to	nephropathy and/or other
				regulate viability and	diseases and disorders as
				proliferation of pancreatic beta	described in the "Renal
_				cells. For example, the Cell	Disorders" section below),
			,	Titer-Glo luminescent cell	diabetic neuropathy, nerve
				viability assay measures the	disease and nerve damage
				number of viable cells in	(e.g., due to diabetic
				culture based on quantitation	neuropathy), blood vessel
				of the ATP present which	blockage, heart disease, stroke,
				signals the presence of	impotence (e.g., due to diabetic
				metabolically active cells.	neuropathy or blood vessel
-				Exemplary assays that may be	blockage), seizures, mental

	used or routinely modified to	confusion, drowsiness,
	test regulation of viability and	nonketotic hyperglycemic-
-	proliferation of pancreatic beta	hyperosmolar coma,
	cells by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Friedrichsen BN,	diseases and disorders as
	et al., Mol Endocrinol,	described in the
	15(1):136-48 (2001); Huotari	"Cardiovascular Disorders"
	MA, et al., Endocrinology,	section below), dyslipidemia,
	139(4):1494-9 (1998); Hugl	endocrine disorders (as
	SR, et al., J Biol Chem 1998	described in the "Endocrine
	Jul 10;273(28):17771-9	Disorders" section below),
	(1998), the contents of each of	neuropathy, vision impairment
	which is herein incorporated	(e.g., diabetic retinopathy and
	by reference in its entirety.	blindness), ulcers and impaired
	Pancreatic cells that may be	wound healing, and infection
	used according to these assays	(e.g., infectious diseases and
	are publicly available (e.g.,	disorders as described in the
	through the ATCC) and/or	"Infectious Diseases" section
	may be routinely generated.	below, especially of the
	Exemplary pancreatic cells that	urinary tract and skin), carpal
	may be used according to these	tunnel syndrome and
	assays include rat INS-1 cells.	Dupuytren's contracture). An
	INS-1 cells are a semi-	additional highly preferred
	adherent cell line established	indication is obesity and/or
	from cells isolated from an X-	complications associated with
	ray induced rat transplantable	obesity. Additional highly
	insulinoma. These cells retain	preferred indications include
	characteristics typical of native	weight loss or alternatively,

				pancreatic beta cells including glucose inducible insulin secretion. References: Asfari	weight gain. Additional highly preferred indications are complications associated with
				et al. Endocrinology 1992 130:167.	insulin resistance.
	HLDQU79	1239	Activation of	Assays for the activation of	A preferred embodiment of
291			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),
				Methods in Enzymol 216:362-	boosting a T cell-mediated
				368 (1992); Henthorn et al.,	immune response, and

suppressing a T cell-mediated immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.
Proc Natl Acad Sci USA 85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.													
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Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the
		Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or
	CD152 in Human T cells	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
	1240	1240
	HLDRM43	HLDRM43
	292	292

	routinely modified to assess	invention includes a method
 	the ability of polypeptides of	for inhibiting endothelial cell
 	the invention (including	growth. A highly preferred
	 antibodies and agonists or	embodiment of the invention
	 antagonists of the invention) to	includes a method for
 	 promote or inhibit cell	stimulating endothelial cell
 	 proliferation, activation, and	proliferation. An alternative
 	apoptosis. Exemplary assays	highly preferred embodiment
	for JNK and p38 kinase	of the invention includes a
	activity that may be used or	method for inhibiting
	routinely modified to test JNK	endothelial cell proliferation.
 	and p38 kinase-induced	A highly preferred
 	activity of polypeptides of the	embodiment of the invention
	invention (including antibodies	includes a method for
 	 and agonists or antagonists of	stimulating apoptosis of
	the invention) include the	endothelial cells. An
 	 assays disclosed in Forrer et	alternative highly preferred
 	al., Biol Chem 379(8-9):1101-	embodiment of the invention
 	1110 (1998); Gupta et al., Exp	includes a method for
 	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	 Soc Symp 64:29-48 (1999);	A highly preferred
 	 Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
 	 Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
 	the contents of each of which	alternative highly preferred
 	are herein incorporated by	embodiment of the invention
 	reference in its entirety.	includes a method for
 	Endothelial cells that may be	inhibiting (e.g., decreasing) the
	 used according to these assays	activation of and/or

ar	are publicly available (e.g.,	inactivating endothelial cells.
	through the ATCC).	A highly preferred
山	Exemplary endothelial cells	embodiment of the invention
thth	that may be used according to	includes a method for
 	these assays include human	stimulating angiogenisis. An
<u>m</u>	umbilical vein endothelial cells	alternative highly preferred
	(HUVEC), which are	embodiment of the invention
	endothelial cells which line	includes a method for
 N .	venous blood vessels, and are	inhibiting angiogenesis. A
 ·ii	involved in functions that	highly preferred embodiment
ui	include, but are not limited to,	of the invention includes a
 ar	angiogenesis, vascular	method for reducing cardiac
	permeability, vascular tone,	hypertrophy. An alternative
ar	and immune cell extravasation.	highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
		hypertrophy. Highly
 	•	preferred indications include
		neoplastic diseases (e.g., as
 		described below under
 		"Hyperproliferative
		Disorders"), and disorders of
		the cardiovascular system
 		(e.g., heart disease, congestive
		heart failure, hypertension,
		aortic stenosis,
 		cardiomyopathy, valvular
 		regurgitation, left ventricular
		dysfunction, atherosclerosis
		and atherosclerotic vascular
		disease, diabetic nephropathy,

intracardiac shunt, cardiac	hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and
																													
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cavernous), glomus tumors, telangiectasia, bacillary angiomatosis,	hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymbhangioma.	lymphangiosarcoma. Highly preferred indications also include cancers such as,	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and	urinary cancer. Preferred indications include benign dysnroliferative disorders and	pre-neoplastic conditions, such as, for example, hyperplasia,	Highly preferred indications also include arterial disease,	such as, atherosclerosis, hypertension, coronary artery disease, inflammatory	vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms,	restenosis; venous and	thrombophlebitis, lymphangitis, and
								<u>.</u>		

						
a; a	and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured	tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation scarring	ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal	diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, oraft rejection, diabetic or	other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders,	age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest,
lyml vasc perij	and prefi inch wou	tissu such ballc athe	ische rheu cerel	dise failu Add indic	othe and vasc angi-	age- dege /prev and Add indic
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heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	
	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess
	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
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the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cell-mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as RANTES, and the induction of chemotactic responses in immune cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J	204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000): Cocchi et al., Science 270(5243):1811-1815 (1995); and Robinson et al., Clin Exp Immunol 101(3):398-407

	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described
which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular tone, and immune cell extravasation.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the
	Activation of transcription through serum response element in immune cells (such as natural killer cells).
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	HLDRM43
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expression of genes involved below under "Immune	he -	function of growth-related Disorders", and/or	 Exemplary assays for Highly preferred indications	transcription through the SRE include autoimmune diseases	that may be used or routinely (e.g., rheumatoid arthritis,	modified to test SRE activity systemic lupus erythematosis,	of the polypeptides of the Crohn's disease, multiple	invention (including antibodies sclerosis and/or as described	and agonists or antagonists of below), immunodeficiencies	the invention) include assays (e.g., as described below),	disclosed in Berger et al., Gene boosting a T cell-mediated	66:1-10 (1998); Cullen and immune response, and	Malm, Methods in Enzymol suppressing a T cell-mediated	216:362-368 (1992); Henthorn immune response. Additional	et al., Proc Natl Acad Sci USA highly preferred indications	85:6342-6346 (1988); Benson include inflammation and	et al., J Immunol 153(9):3862- inflammatory disorders, and	l.,	Virus Genes 12(2):105-117 patients with rheumatoid	(1997), the content of each of arthritis. An additional highly	which are herein incorporated preferred indication is sepsis.	by reference in its entirety. T Highly preferred indications	cells that may be used include neoplastic diseases	's are	publicly available (e.g., and/or as described below	through the ATCC). under "Hyperproliferative	Exemplary T cells that may be Disorders"). Additionally,	used according to these assays highly preferred indications	include the MK_VT call line include neonleams and

	which is a human natural killer	cancers such as for example
	coll line with court its and	l1
	cell line with cytolytic and	leukemia, lympnoma,
	cytotoxic activity.	melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
 		esophageal, stomach, brain,
 		liver and urinary cancer. Other
 		preferred indications include
		benign dysproliferative
 		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
		anemia, pancytopenia,
 		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
 		plasmacytomas, multiple
 		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
 		organs and tissues, hemophilia,
 		hypercoagulation, diabetes
		mellitus, endocarditis,
		meningitis, Lyme Disease,

					cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
292	HLDRM43	1240	Activation of transcription through CD28	Assays for the activation of transcription through the CD28 response element are well-	A highly preferred embodiment of the invention includes a method for
			response element in immune cells (such as T-cells).	known in the art and may be used or routinely modified to assess the ability of	stimulating T cell proliferation. An alternative highly preferred embodiment of the invention
				(including antibodies and agonists or antagonists of the	includes a method for inhibiting T cell proliferation. A highly preferred
			,	expression in T cells. Exemplary assays for transcription through the CD28	includes a method for activating T cells. An alternative highly preferred
				response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies	embodiment or the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred
				and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	embodiment of the invention includes a method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment
				216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	of the invention includes a method for inhibiting (e.g.,

			85:6342-6346 (1988);	reducing) IL-2 production.
	100		McGuire and Iacobelli, J	Additional highly preferred
			Immunol 159(3):1319-1327	indications include
			(1997); Parra et al., J Immunol	inflammation and
			166(4):2437-2443 (2001); and	inflammatory disorders.
			Butscher et al., J Biol Chem	Highly preferred indications
			3(1):552-560 (1998), the	include autoimmune diseases
			contents of each of which are	(e.g., rheumatoid arthritis,
			herein incorporated by	systemic lupus erythematosis,
			reference in its entirety. T	multiple sclerosis and/or as
			cells that may be used	described below),
			according to these assays are	immunodeficiencies (e.g., as
			publicly available (e.g.,	described below), boosting a T
			through the ATCC).	cell-mediated immune
			Exemplary human T cells that	response, and suppressing a T
10			may be used according to these	cell-mediated immune
			assays include the SUPT cell	response. Highly preferred
			line, which is a suspension	indications include neoplastic
·			culture of IL-2 and IL-4	diseases (e.g., melanoma, renal
			responsive T cells.	cell carcinoma, leukemia,
				lymphoma, and/or as described
				below under
				"Hyperproliferative
				Disorders"). Highly preferred
				indications include neoplasms
				and cancers, such as, for
				example, melanoma (e.g.,
				metastatic melanoma), renal
				cell carcinoma (e.g., metastatic
				renal cell carcinoma),
				leukemia, lymphoma (e.g., T

breast, Jung, colon, parpetatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication includes infection (e.g., AIDS, tuberculosis, infections disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indication is AIDS. Additional highly preferred indications include engans and/or itssues, and and/or itssues, wreitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Inmune Activity", "Blood-Lannune Activity", "Blood-Related Disorders"), "Cardiovascular Disorders").				cell lymphoma) and prostate
esophageal, stonach, be liver and urinary cancer preferred indications in benign dysproliferative disorders and pre-neoplicative disorders and continuous disorders and continuous disorders in disorders in disorders and continuous disorders and continuous disorders and continuous disorders disorders disorders disorders disorders disorders disorders disorders disorders and continuous disorders (e.g., as describele) disorders (e.g., as describele) disorders, and or and disorders (e.g., as describele) disorders, and or "Immune Activity", "Blood-Relat Disorders", and or "Cardiovascular Disorders", and				hreast ling colon pancreation
lesophageal, stomach, bleschend indications in preferred indications in preferred indications in penign dysproliferative disorders and pre-neople conditions, such as, for example, hyperplasia, metaplasia, and/or dyspl A highly preferred indication in associated with granuloi disease, and osteoporosi and/or as described belo under "Infection Disease, inghly preferred indications in suppression of immune reactions to transplante organs and/or tissues, up psortiasis, and tropical si paraparesis. Preferred indications in transplante organs and/or tissues, up psortiasis, and tropical si paraparesis. Preferre indications include bloo disorders (e.g., as described below under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord". "Cardiovascular Disord"				oreast, fung, colon, pancreatic,
liver and urinary cancer preferred indications in bening dysproliferative disorders and pre-neople conditions, such as, for example, hyperplasia, metaplasia, and/or dysplotiferative disorders and pre-neople conditions, such as, for example, hyperplasia, metaplasia, and/or dysplotiferative disorders infection (e.g., highly preferred indication in disease, and osteoporosi and or as described below under "Infectious Diseaship preferred indication in preferred indications in suppression of immune reactions to transplanted organs and/or tissues, ur psoriasis, and tropical sip paraparesis. Preferre paraparesis, "Blood-Relat pisorders", "allod-Relat Disorders", "and/or "Cardiovascular Disord". "Cardiovascular Disorder"				esophageal, stomach, brain,
preferred indications in beniga dysproliferative disorders and pre-neoph conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia, metaplasia, and/or dysplasia, metaplasia, and/or dysplasia, includes infection (e.g., AIDS, tuberculosis, infeases, and osteoperosi and/or as described belounder "Infectious Disease und osteoperosi and/or as described belounder "Infectious Disease und osteoperosi and/or infeasions in immune reactions to transplantec organs and/or tissues, ur poropression of immune reactions include bloo disorders (e.g., as described below under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord" "Cardiovascular Disord"		_		liver and urinary cancer. Other
henign dysproliferative disorders and pre-neople conditions, such as, for example, hyperplasia, metaphasia, and or dyspl A highly preferred indic includes infection (e.g., AIDS, tuberculosis, infe associated with granuloi disease, and osteoprosis, and/or as described belo under "Infectious Disea highly preferred indications infe preferred indications in or suppression of immune reactions to transplantec organs and/or issues, ur psoriasis, and tropical si paraparesis. Preferre indications include bloo disorders (e.g., as descri below under "Inmune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord	-			preferred indications include
disorders and pre-neopla conditions, such as, for example, hyperplasia, metaplasia, and/or dyspl A highly preferred indiciniculdes infection (e.g., AIDS, tuberculosis, infe associated with granuloi disease, and osteoporosi and/or as described belo under "Infectious Disease, highly preferred indicati AIDS. Additional high preferred indications in suppression of immune reactions to transplanted organs and/or tissues, up psoriasis, and tropical si paraparesis. Preferre indications include bloo disorders (e.g., as described below under "Immune Activity", "Blood-Relat Disorder", "and/or "Cardiovascular Disord" "Cardiovascular Disord"				benign dysproliferative
conditions, such as, for example, hyperplasia, metaplasia, and/or dyspl A highly preferred indicincludes infection (e.g., AIDS, tuberculosis, infeasosciated with granulor disease, and osteoporosis and/or as described belounder "Infectious Diseasinghly preferred indications in suppression of immune reactions to transplanter organs and/or tissues, upportisatis, and tropical sippression of immune reactions to transplante organs and/or tissues, upsoriasis, and tropical sippressions indications include bloo disorders (e.g., as describely under "Inmume Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord" "Cardiovascular Disord				disorders and pre-neoplastic
example, hyperplasia, metaplasia, and/or dyspl A highly preferred indic includes infection (e.g., AIDS, tuberculosis, infe associated with granulou disease, and osteoporosi and/or as described belo under "Infectious Disea, highly preferred indicati AIDS. Additional high preferred indications to transplanted organs and/or tissues, urpsoriasis, and tropical sip paraparesis. Preferre indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disorder", "Cardiovascular Disorder", "Cardiovascular Disorders", and/or		_		conditions, such as, for
metaplasia, and/or dyspl A highly preferred indic includes infection (e.g., AIDS, tuberculosis, infe associated with granuloi disease, and osteoporosis and/or as described belo under "Infectious Diseas" highly preferred indicati AIDS. Additional high preferred indications in suppression of immune reactions to transplantec organs and/or tissues, ur psoriasis, and tropical si paraparesis. Preferre indications include bloo disorders (e.g., as describ below under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord				example, hyperplasia,
A highly preferred indication (e.g., AIDS, tuberculosis, infeases, and osteoporosi and/or as described belo under "Infectious Disca highly preferred indicational high preferred indicational high preferred indications in suppression of immune reactions to transplante organs and/or tissues, ur psoriasis, and tropical sy paraparesis. Preferre indications include bloo disorders (e.g., as descri below under "Immune Activity," "Blood-Relat Disorders", and/or "Cardiovascular Disord				metaplasia, and/or dysplasia.
includes infection (e.g., AIDS, tuberculosis, infe associated with granulor disease, and osteoporosi and/or as described belo under "Infectious Disea highly preferred indicational high preferred indicational high preferred indications inc suppression of immune reactions to transplantec organs and/or tissues, ur psoriasis, and tropical si paraparesis. Preferre indications include bloo disorders (e.g., as descri below under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord				A highly preferred indication
AIDS, tuberculosis, infe associated with granulor disease, and osteoporosi and/or as described belo under "Infectious Diseas highly preferred indicati preferred indications in suppression of immune reactions to transplanted organs and/or tissues, upsoriasis, and tropical sip paraparesis. A perferred indications include bloo disorders (e.g., as describelow under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disorder "Cardiovascular Disorder "Cardiovascular Disorder"				includes infection (e.g.,
associated with granulor disease, and osteoporosi and/or as described belo under "Infectious Diseas highly preferred indicati AIDS. Additional high preferred indications in suppression of immune reactions to transplantec organs and/or tissues, ur psoriasis, and tropical sy paraparesis. Preferre indications include bloo disorders (e.g., as descri below under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord	-	, , ,		AIDS, tuberculosis, infections
disease, and osteoporosi and/or as described belo under "Infectious Diseas highly preferred indicati AIDS. Additional high preferred indications ins suppression of immune reactions to transplantec organs and/or tissues, ur psoriasis, and tropical st paraparesis. Preferre indications include bloo disorders (e.g., as descri below under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord				associated with granulomatous
and/or as described belo under "Infectious Diseas highly preferred indicati AIDS. Additional high preferred indications inc suppression of immune reactions to transplantec organs and/or tissues, ur psoriasis, and tropical st paraparesis. Preferre indications include bloo disorders (e.g., as descri below under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord				disease, and osteoporosis,
under "Infectious Diseas highly preferred indication highly preferred indications in suppression of immune reactions to transplanted organs and/or tissues, upportants, and tropical syparaparesis. Preferre indications include blood disorders (e.g., as describelow under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord				and/or as described below
highly preferred indicational high preferred indications in suppression of immune reactions to transplanted organs and/or tissues, upsoriasis, and tropical syparaparesis. Preferre indications include blood disorders (e.g., as describelow under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord	_			under "Infectious Disease"). A
AIDS. Additional high preferred indications in suppression of immune reactions to transplantec organs and/or tissues, up psoriasis, and tropical styparaparesis. Preferre indications include bloo disorders (e.g., as describelow under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord				highly preferred indication is
preferred indications inc suppression of immune reactions to transplantec organs and/or tissues, u) psoriasis, and tropical si paraparesis. Preferre indications include bloo disorders (e.g., as descri below under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord				AIDS. Additional highly
suppression of immune reactions to transplanted organs and/or tissues, ur psoriasis, and tropical sy paraparesis. Preferre indications include bloo disorders (e.g., as descri below under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord				preferred indications include
reactions to transplanted organs and/or tissues, uv psoriasis, and tropical sparaparesis. Preferre indications include bloo disorders (e.g., as describelow under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disorda				suppression of immune
organs and/or tissues, uv psoriasis, and tropical sy paraparesis. Preferre indications include bloo disorders (e.g., as describelow under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disorder Disor				reactions to transplanted
psoriasis, and tropical sparaparesis. Preferre indications include bloo disorders (e.g., as describelow under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disordia Disord				organs and/or tissues, uveitis,
paraparesis. Preferre indications include bloo disorders (e.g., as descri below under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord				psoriasis, and tropical spastic
indications include bloo disorders (e.g., as describelow under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disorder				paraparesis. Preferred
disorders (e.g., as describelow under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disordiar D				indications include blood
below under "Immune Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disord		-		disorders (e.g., as described
Activity", "Blood-Relat Disorders", and/or "Cardiovascular Disorder				below under "Immune
Disorders", and/or "Cardiovascular Disorders"				Activity", "Blood-Related
"Cardiovascular Disorde				Disorders", and/or
				"Cardiovascular Disorders").

S H H J H G G G R H P J V T T G H P S	tion of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune below under "Immune disorders", "Blood-Related bloord disorders", and/or "Cardiovascular Disorders").
	Assays for the activation of transcription through the Serum Response Element in (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or
	Activation of transcription through serum response element in immune cells (such as T-cells).
	1241
	HLDRP33
	293

	routinely modified to test SRE	Highly preferred indications
	activity of the polypeptides of	include autoimmune diseases
	the invention (including	(e.g., rheumatoid arthritis,
	antibodies and agonists or	systemic lupus erythematosis,
	antagonists of the invention)	Crohn"s disease, multiple
	include assays disclosed in	sclerosis and/or as described
	Berger et al., Gene 66:1-10	below), immunodeficiencies
,	(1998); Cullen and Malm,	(e.g., as described below),
	Methods in Enzymol 216:362-	boosting a T cell-mediated
	368 (1992); Henthorn et al.,	immune response, and
	Proc Natl Acad Sci USA	suppressing a T cell-mediated
	85:6342-6346 (1988); and	immune response. Additional
	Black et al., Virus Genes	highly preferred indications
	12(2):105-117 (1997), the	include inflammation and
	content of each of which are	inflammatory disorders, and
	herein incorporated by	treating joint damage in
	reference in its entirety. T	patients with rheumatoid
	cells that may be used	arthritis. An additional highly
	according to these assays are	preferred indication is sepsis.
	publicly available (e.g.,	Highly preferred indications
 	through the ATCC).	include neoplastic diseases
	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
	may be used according to these	and/or as described below
	assays include the CTLL cell	under "Hyperproliferative
	line, which is an IL-2	Disorders"). Additionally,
	dependent suspension culture	highly preferred indications
	of T cells with cytotoxic	include neoplasms and
	activity.	cancers, such as, for example,
		leukemia, lymphoma,
		melanoma, glioma (e.g.,
		malignant glioma), solid

tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication	is infection (e.g., an infectious
				·																										

disease as described below under "Infectious Disease").	Preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), blood disorders	(e.g., as described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), and infection	(e.g., an infectious disease as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under
	Kinase assay. JNK and p38	kinase assays for signal	transduction that regulate cell	proliferation, activation, or	apoptosis are well known in	the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	promote or inhibit immune cell	(e.g. T-cell) proliferation,	activation, and apoptosis.	Exemplary assays for JNK and	p38 kinase activity that may be	used or routinely modified to	test JNK and p38 kinase-	induced activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Forrer et al., Biol	Chem 379(8-9):1101-1110	(1998); Gupta et al., Exp Cell	Res 247(2): 495-504 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang
	Activation of T-	Cell p38 or JNK	Signaling Pathway.																										
	1242																												
	HLHFP03																												
		294							,																				

				and Karin. Nature	"Hyperproliferative
				410(6824):37-40 (2001); and	Disorders"). Highly preferred
				Cobb MH, Prog Biophys Mol	indications include neoplasms
	·			Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
				the contents of each of which	lymphoma, prostate, breast,
				are herein incorporated by	lung, colon, pancreatic,
				reference in its entirety. T	esophageal, stomach, brain,
				cells that may be used	liver, and urinary cancer. Other
				according to these assays are	preferred indications include
				publicly available (e.g.,	benign dysproliferative
				through the ATCC).	disorders and pre-neoplastic
				Exemplary mouse T cells that	conditions, such as, for
				may be used according to these	example, hyperplasia,
	18			assays include the CTLL cell	metaplasia, and/or dysplasia.
				line, which is an IL-2	Preferred indications include
				dependent suspension-culture	arthritis, asthma, AIDS,
				cell line with cytotoxic	allergy, anemia, pancytopenia,
·				activity.	leukopenia, thrombocytopenia,
					Hodgkin"s disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
294	HLHFP03	1242	SEAP in HIB/CRE		
	HLHFP03	1242	VEGF in HT1080		

294					
700	HLHFP03	1242	Production of	Assays for measuring	Highly preferred indications
294			VCAM in	expression of VCAM are well-	include inflammation (acute
			endothelial cells	known in the art and may be	and chronic), restnosis,
			(such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
			endothelial cells	polypeptides of the invention	indications include
			(HUVEC))	(including antibodies and	inflammation and
				agonists or antagonists of the	inflammatory disorders,
•			-	invention) to regulate VCAM	immunological disorders,
				expression. For example,	neoplastic disorders (e.g.
				FMAT may be used to meaure	cancer/tumorigenesis), and
				the upregulation of cell surface	cardiovascular disorders (such
				VCAM-1 expresssion in	as described below under
				endothelial cells. Endothelial	"Immune Activity", "Blood-
				cells are cells that line blood	Related Disorders",
				vessels, and are involved in	"Hyperproliferative Disorders"
				functions that include, but are	and/or "Cardiovascular
				not limited to, angiogenesis,	Disorders"). Highly preferred
				vascular permeability, vascular	indications include neoplasms
				tone, and immune cell	and cancers such as, for
				extravasation. Exemplary	example, leukemia, lymphoma,
				endothelial cells that may be	melanoma, renal cell
				used according to these assays	carcinoma, and prostate,
				include human umbilical vein	breast, lung, colon, pancreatic,
				endothelial cells (HUVEC),	esophageal, stomach, brain,
				which are available from	liver and urinary cancer. Other
				commercial sources. The	preferred indications include
				expression of VCAM	benign dysproliferative
				(CD106), a membrane-	disorders and pre-neoplastic
				associated protein, can be	conditions, such as, for

	upregulated by cytokines or example, hyperplasia, other factors, and contributes metaplasia, and/or dysplasia. to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.		TNFa FMAT. Assays for	by dendritic immunomodulatory proteins	produced by activated includes a method for macrophage T cells inhibiting (e.g. decreasing)	uscle,	rt a	wide variety of inflammatory embodiment of the invention	and cytotoxic effects on a includes a method for	variety of cells are well known stimulating (e.g., increasing)			es of	. ,		antagonists of the invention) to Related Disorders", and/or	mediate immunomodulation, "Cardiovascular Disorders"),	modulate inflammation and Highly preferred indications	cytotoxicity. Exemplary include autoimmune diseases	assays that test for (e.g., rheumatoid arthritis,	imminomodulatory proteins systemic lunis erythematosis
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				assays may be isolated using	benign dysproliferative
				techniques disclosed herein or	disorders and pre-neoplastic
,				otherwise known in the art.	conditions, such as, for
				Human dendritic cells are	example, hyperplasia,
·				antigen presenting cells in	metaplasia, and/or dysplasia.
				suspension culture, which,	Preferred indications include
				when activated by antigen	anemia, pancytopenia,
				and/or cytokines, initiate and	leukopenia, thrombocytopenia,
				upregulate T cell proliferation	Hodgkin's disease, acute
				and functional activities.	lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
			-		neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
1	HLHFR58	1243	RANTES in		
295			Human I cells		
	HLIBD68	1244	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred

962	by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and increases lgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate	embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
	immunomodulation and differentiation and modulate T	immunodeficiencies (e.g., as
	cell proliferation and function. Exemplary assays that test for	preferred indications also include boosting a B cell-
	immunomodulatory proteins	mediated immune response

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and alternatively suppressing a B cell-mediated immune response. Highly preferred indications include inflammation and	inflammatory disorders. Additional highly preferred indications include asthma and allergy. Highly	preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma, leukemia, lymphoma,	melanoma, and/or as described below under "Hyperproliferative Disorders" Highly preferred	indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include
evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional	activities. Such assays that may be used or routinely modified to test immunomodulatory and	diffferentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-	"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925	(1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these	assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in

suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. Imphoma, arthritis, AIDS, granulomatory bowel disease, sepsis, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infectious Disease").	MIP-lalpha FMAT. Assays MIP lalpha for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T and may be lincludes a method for embodiment of the invention known in the art and may be lincludes a method for includes a method for sassess the ability of MIP la production. A highly
	HLIBD68 1244 Pr
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infection (e.g., an infectious	disease as described below	under "Infectious Disease").	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,
(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, modulate	chemotaxis, and modulate T	cell differentiation. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	chemokines, such as	macrophage inflammatory	protein 1 alpha (MIP-1a), and	the activation of	monocytes/macrophages and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	chemotaxis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and	Eremin, J R Coll Surg Ednb	45(1):9-19 (2001); Drakes et	al., Transp Immunol 8(1):17-
				-																										
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				29 (2000); Verhasselt et al., J	suppression of immune
				Immunol 158:2919-2925	reactions to transplanted
				(1997); and Nardelli et al., J	organs and tissues, hemophilia,
				Leukoc Biol 65:822-828	hypercoagulation, diabetes
				(1999), the contents of each of	mellitus, endocarditis,
				which are herein incorporated	meningitis, Lyme Disease,
				by reference in its entirety.	asthma, and allergy.
				Human dendritic cells that may	Preferred indications also
				be used according to these	include neoplastic diseases
				assays may be isolated using	(e.g., leukemia, lymphoma,
				techniques disclosed herein or	and/or as described below
				otherwise known in the art.	under "Hyperproliferative
				Human dendritic cells are	Disorders"). Highly preferred
				antigen presenting cells in	indications include neoplasms
				suspension culture, which,	and cancers, such as, leukemia,
				when activated by antigen	lymphoma, prostate, breast,
				and/or cytokines, initiate and	lung, colon, pancreatic,
•				upregulate T cell proliferation	esophageal, stomach, brain,
	-			and functional activities.	liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HLIBD68	1244	Production of TNF	TNFa FMAT. Assays for	A highly preferred
296			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
	-			macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred

		annrach" Chanter 6:138-160	le a leukemia lymnhoma
	***	appropriate compression of the control of the contr	(c.s., reascina, 1) inplicana,
		(2000); Verhasselt et al., Eur J	and/or as described below
		Immunol 28(11):3886-3890	under "Hyperproliferative
		(1198); Dahlen et al., J	Disorders"). Additionally,
		Immunol 160(7):3585-3593	highly preferred indications
		(1998); Verhasselt et al., J	include neoplasms and
		Immunol 158:2919-2925	cancers, such as, leukemia,
-		(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
		Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
		(1999), the contents of each of	tumors, and prostate, breast,
		which are herein incorporated	lung, colon, pancreatic,
		by reference in its entirety.	esophageal, stomach, brain,
		Human dendritic cells that may	liver and urinary cancer. Other
		be used according to these	preferred indications include
		assays may be isolated using	benign dysproliferative
		techniques disclosed herein or	disorders and pre-neoplastic
		otherwise known in the art.	conditions, such as, for
		Human dendritic cells are	example, hyperplasia,
		antigen presenting cells in	metaplasia, and/or dysplasia.
	•	suspension culture, which,	Preferred indications include
		when activated by antigen	anemia, pancytopenia,
		and/or cytokines, initiate and	leukopenia, thrombocytopenia,
	-	upregulate T cell proliferation	Hodgkin's disease, acute
		and functional activities.	lymphocytic anemia (ALL),
			plasmacytomas, multiple
	444		myeloma, Burkitt's lymphoma,
	-11		arthritis, AIDS, granulomatous
			disease, inflammatory bowel
			disease, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune

				reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
HLIBD68 1244	4	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel

	used or routinely modified to	confusion, drowsiness,
	test for stimulation of insulin	nonketotic hyperglycemic-
	secretion (from pancreatic	hyperosmolar coma,
	cells) by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Ahren, B., et al.,	diseases and disorders as
	Am J Physiol, 277(4 Pt	described in the
	2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
	al., Endocrinology,	section below), dyslipidemia,
	138(9):3735-40 (1997); Kim,	endocrine disorders (as
	K.H., et al., FEBS Lett,	described in the "Endocrine
	377(2):237-9 (1995); and,	Disorders" section below),
	Miraglia S et. al., Journal of	neuropathy, vision impairment
	Biomolecular Screening,	(e.g., diabetic retinopathy and
	4:193-204 (1999), the contents	blindness), ulcers and impaired
	of each of which is herein	wound healing, and infection
	incorporated by reference in its	(e.g., infectious diseases and
	entirety. Pancreatic cells that	disorders as described in the
	may be used according to these	"Infectious Diseases" section
	assays are publicly available	below, especially of the
	(e.g., through the ATCC)	urinary tract and skin), carpal
	and/or may be routinely	tunnel syndrome and
	generated. Exemplary	Dupuytren's contracture).
	pancreatic cells that may be	An additional highly preferred
	used according to these assays	indication is obesity and/or
	include rat INS-1 cells. INS-1	complications associated with
	cells are a semi-adherent cell	obesity. Additional highly
	line established from cells	preferred indications include
	isolated from an X-ray induced weight loss or alternatively,	weight loss or alternatively,

				rat transplantable insulinoma. These cells retain	weight gain. Aditional highly preferred indications are
				characteristics typical of native pancreatic beta cells including	complications associated with insulin resistance.
				glucose inducible insulin	
				secretion. References: Asfari	
				et al. Endocrinology 1992	
	HLICQ90	1245	Activation of	Assays for the activation of	A preferred embodiment of
297			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies

(e.g., as described below), boosting a T cell-mediated immune response, and	suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and	inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly	preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below	under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example,	leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast,	lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic
(1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the	content of each of which are herein incorporated by reference in its entirety. T cells that may be used	according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these	assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	•	

					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
-					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
	*				neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
				J	disease as described below
					under "Infectious Disease").
H	нгісо90	1245	Production of TNF	TNFa FMAT. Assays for	A highly preferred
			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An

B	ory	 <u> </u>	 routinely modified to assess Highly preferred indications	Jo se	the invention (including as described below under	ı	n) to	mediate immunomodulation, "Cardiovascular Disorders"),	modulate inflammation and Highly preferred indications	cytotoxicity. Exemplary include autoimmune diseases	assays that test for (e.g., rheumatoid arthritis,	immunomodulatory proteins systemic lupus erythematosis,	evaluate the production of Crohn's disease, multiple	cytokines such as tumor sclerosis and/or as described	necrosis factor alpha (TNFa), below), immunodeficiencies	and the induction or inhibition (e.g., as described below),	of an inflammatory or boosting a T cell-mediated	cytotoxic response. Such immune response, and	assays that may be used or suppressing a T cell-mediated	routinely modified to test immune response. Additional	immunomodulatory activity of highly preferred indications	polypeptides of the invention include inflammation and	(including antibodies and inflammatory disorders, and	agonists or antagonists of the treating joint damage in	invention) include assays patients with rheumatoid	disclosed in Miraglia et al., J arthritis. An additional highly	Biomolecular Screening 4:193- preferred indication is sepsis.	

"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	
				091	(2000); Verhasselt et al., Eur J	Immunol 28(11):3886-3890	(1198); Dahlen et al., J	Immunol 160(7):3585-3593	(1998); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of					assays may be isolated using			Human dendritic cells are		suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.	-				

suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	the art indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., tibodies diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel ading to hockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel
	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium
	Stimulation of Calcium Flux in pancreatic beta cells.
	1245
	HLICQ90
	297

	and alterations in cell	blockage), seizures, mental
	functions. Exemplary assays	confusion, drowsiness,
	that may be used or routinely	nonketotic hyperglycemic-
-	modified to measure calcium	hyperosmolar coma,
	flux by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Satin LS, et al.,	diseases and disorders as
	Endocrinology, 136(10):4589-	described in the
	601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
	Endocrinology, 136(7):2960-6	section below), dyslipidemia,
	(1995); Richardson SB, et al.,	endocrine disorders (as
	Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
	(1992); and, Meats, JE, et al.,	Disorders" section below),
	Cell Calcium 1989 Nov-	neuropathy, vision impairment
	Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
	contents of each of which is	blindness), ulcers and impaired
	herein incorporated by	wound healing, and infection
	reference in its entirety.	(e.g., infectious diseases and
	Pancreatic cells that may be	disorders as described in the
	used according to these assays	"Infectious Diseases" section
	are publicly available (e.g.,	below, especially of the
	through the ATCC) and/or	urinary tract and skin), carpal
	may be routinely generated.	
	Exemplary pancreatic cells that	
	may be used according to these	An additional highly preferred
	assays include HITT15 Cells.	indication is obesity and/or
	HITT15 are an adherent	complications associated with
	epithelial cell line established	obesity. Additional highly
	from Syrian hamster islet cells	preferred indications include

				transformed with SV40. These	weight loss or alternatively,
				cells express glucagon,	weight gain. Aditional
				somatostatin, and	highly preferred indications are
<u></u>				glucocorticoid receptors. The	complications associated with
				cells secrete insulin, which is	insulin resistance.
				stimulated by glucose and	
				glucagon and suppressed by	
				somatostatin or	
			,	glucocorticoids. ATTC# CRL-	
				1777 Refs: Lord and	
				Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc.	
				Natl. Acad. Sci. USA 78:	
		,		4339-4343, 1981.	
	HLICQ90	1245	Stimulation of	Assays for measuring secretion	A highly preferred
297			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
			from pancreatic	the art and may be used or	An additional highly preferred
			beta cells.	routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic
				also by certain	neuropathy), blood vessel
				proteins/peptides, and	blockage, heart disease, stroke,

impotence (e.g., due to diabetic	neuropathy or blood vessel	be blockage), seizures, mental			hyperosmolar coma,		ies		/s hypertension, stroke, and other	il., diseases and disorders as	described in the	et "Cardiovascular Disorders"	section below), dyslipidemia,		described in the "Endocrine	Disorders" section below),	f neuropathy, vision impairment	(e.g., diabetic retinopathy and	ents blindness), ulcers and impaired	wound healing, and infection			nese "Infectious Diseases" section	e below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	ays indication is obesity and/or	
disregulation is a key	component in diabetes.	Exemplary assays that may be	used or routinely modified to	test for stimulation of insulin	secretion (from pancreatic	cells) by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Ahren, B., et al.,	Am J Physiol, 277(4 Pt	2):R959-66 (1999); Li, M., et	al., Endocrinology,	138(9):3735-40 (1997); Kim,	K.H., et al., FEBS Lett,	377(2):237-9 (1995); and,	Miraglia S et. al., Journal of	Biomolecular Screening,	4:193-204 (1999), the contents	of each of which is herein	incorporated by reference in its	entirety. Pancreatic cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC)	and/or may be routinely	generated. Exemplary	pancreatic cells that may be	used according to these assays	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
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														-																

				cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
				These cells retain	highly preferred indications are
	-			characteristics typical of native	complications associated with
				pancreatic beta cells including	insulin resistance.
			-	glucose inducible insulin	
				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	
	HLMB076	1246	Activation of	Assays for the activation of	A preferred embodiment of
298			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
		1		modified to test SRE activity	systemic lupus erythematosis,

jo	of the polypeptides of the	Crohn's disease, multiple
NOT .	invention (including antibodies	sclerosis and/or as described
an	and agonists or antagonists of	below), immunodeficiencies
the	the invention) include assays	(e.g., as described below),
dis	disclosed in Berger et al., Gene	boosting a T cell-mediated
99	66:1-10 (1998); Cullen and	immune response, and
W	Malm, Methods in Enzymol	suppressing a T cell-mediated
21	216:362-368 (1992); Henthorn	immune response. Additional
et	et al., Proc Natl Acad Sci USA	highly preferred indications
85	85:6342-6346 (1988); Benson	include inflammation and
et	et al., J Immunol 153(9):3862-	inflammatory disorders, and
38	3873 (1994); and Black et al.,	treating joint damage in
	Virus Genes 12(2):105-117	patients with rheumatoid
	(1997), the content of each of	arthritis. An additional highly
W	which are herein incorporated	preferred indication is sepsis.
by	by reference in its entirety. T	Highly preferred indications
93	cells that may be used	include neoplastic diseases
ac	according to these assays are	(e.g., leukemia, lymphoma,
nd	publicly available (e.g.,	and/or as described below
thr	through the ATCC).	under "Hyperproliferative
	Exemplary T cells that may be	Disorders"). Additionally,
sn	used according to these assays	highly preferred indications
in i	include the NK-YT cell line,	include neoplasms and
Iw	which is a human natural killer	cancers, such as, for example,
93	cell line with cytolytic and	leukemia, lymphoma,
cy	cytotoxic activity.	melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other

					Some frame of the discontinue in already
			_		picielled marcanons menue
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
			-		Hodgkin's disease, acute
					lymphocytic anemia (ALL),
-					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues, hemophilia,
			-		hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HLQBE09	1247	Production of IL-8	Assay that measures the	Highly preferred indications
667			by immune cells	production of the chemokine	include eosinophilia, asthma,

(such as the human
EOL-1 eosinophil
cells)
SEAP in HIB/CRE

	HLQBE09	1247	CD71 in Human T cells		
	НГОВЕ09	1247	IL-10 in Human T-cell 293T		
	HLQBE09	1247	TNFa in Human T- cell 2B9		
	HLQDR48	1248	Activation of Adipocyte ERK	Kinase assay. Kinase assays, for example an Elk-1 kinase	A highly preferred embodiment of the invention
			Signaling Pathway	assay, for EKK signal transduction that regulate cell	includes a method for stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or rounnery modified to assess the ability	or the invention includes a method for inhibiting
				of polypeptides of the	adipocyte proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a
				the invention) to promote or	method for stimulating
				inhibit cell proliferation,	adipocyte differentiation. An
				activation, and differentiation.	alternative highly preferred
				Exemplary assays for ERK	embodiment of the invention
		71.		kinase activity that may be	includes a method for
				used or routinely modified to	inhibiting adipocyte
				test ERK kinase-induced	differentiation. A highly
		•		activity of polypeptides of the	preferred embodiment of the
				invention (including antibodies	invention includes a method
				and agonists or antagonists of	for stimulating (e.g.,
				the invention) include the	increasing) adipocyte
				assays disclosed in Forrer et	activation. An alternative
}				al., Biol Chem 379(8-9):1101-	highly preferred embodiment

														_											
of the invention includes a method for inhibiting the activation of (e.g., decreasing)	and/or inactivating adipocytes. Highly preferred indications	include endocrine disorders (e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	described below under	"Hyperproliferative	Disorders"). Preferred	indications include blood	disorders (e.g., hypertension,	congestive heart failure, blood	vessel blockage, heart disease,	stroke, impotence and/or as	described below under	'"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as
1110 (1998); Le Marchand- Brustel Y, Exp Clin Endocrinol Diabetes	107(2):126-132 (1999); Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang and Karin. Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	reference in its entirety.	Mouse adipocyte cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.	
											-			-									-		
																								-	

_		described below under
		described below dides
		"Infectious Disease").
		A highly preferred indication
		is diabetes mellitus. An
	-	additional highly preferred
		indication is a complication
		associated with diabetes (e.g.,
		diabetic retinopathy, diabetic
		nephropathy, kidney disease
		(e.g., renal failure,
		nephropathy and/or other
		diseases and disorders as
		described in the "Renal
		Disorders" section below),
		diabetic neuropathy, nerve
		disease and nerve damage
	~	(e.g., due to diabetic
		neuropathy), blood vessel
		blockage, heart disease, stroke,
		impotence (e.g., due to diabetic
		neuropathy or blood vessel
		blockage), seizures, mental
		confusion, drowsiness,
		nonketotic hyperglycemic-
		hyperosmolar coma,
		cardiovascular disease (e.g.,
		heart disease, atherosclerosis,
		microvascular disease,
		hypertension, stroke, and other
		diseases and disorders as
		described in the

"Cardiovascular Disorders"	section below), dyslipidemia, endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein
		-						,																				

					indications include,
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					hypertension, coronary artery disease dyslinidemia
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					gallstones, osteoarthritis,
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					degenerative arthritis, eating
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					disorders, fibrosis, cachexia,
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					and kidney diseases or
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					disorders. Preferred
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					indications include neoplasms
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					and cancer, such as,
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					lymphoma, leukemia and
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					breast, colon, and kidney
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					cancer. Additional preferred
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T			·		indications include melanoma,
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					prostate, lung, pancreatic,
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					esophageal, stomach, brain,
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					liver, and urinary cancer.
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					Highly preferred indications
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T			-		include lipomas and
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					liposarcomas. Other preferred
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					indications include benign
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					dysproliferative disorders and
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T			.		pre-neoplastic conditions, such
Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T					as, for example, hyperplasia,
MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T	\dashv				metaplasia, and/or dysplasia.
immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T		1248	Production of	MCP-1 FMAT. Assays for	A highly preferred
			MCP-1	immunomodulatory proteins	embodiment of the invention
				that are produced by a large	includes a method for
				variety of cells and act to	stimulating (e.g., increasing)
				induce chemotaxis and	MCP-1 production. An
4				activation of monocytes and T	alternative highly preferred

		cells are well known in the art	embodiment of the invention
		and may be used or routinely	includes a method for
		modified to assess the ability	inhibiting (e.g., reducing)
		of polypeptides of the	MCP-1 production. A highly
		invention (including antibodies	preferred indication is
		and agonists or antagonists of	infection (e.g., an infectious
		the invention) to mediate	disease as described below
		immunomodulation, induce	under "Infectious Disease").
		chemotaxis, and modulate	Additional highly preferred
		immune cell activation.	indications include
		Exemplary assays that test for	inflammation and
		immunomodulatory proteins	inflammatory disorders.
		evaluate the production of cell	Preferred indications include
		surface markers, such as	blood disorders (e.g., as
		monocyte chemoattractant	described below under
		protein (MCP), and the	"Immune Activity", "Blood-
		activation of monocytes and T	Related Disorders", and/or
		cells. Such assays that may be	"Cardiovascular Disorders").
		used or routinely modified to	Highly preferred indications
		test immunomodulatory and	include autoimmune diseases
		diffferentiation activity of	(e.g., rheumatoid arthritis,
		polypeptides of the invention	systemic lupus erythematosis,
		(including antibodies and	multiple sclerosis and/or as
		agonists or antagonists of the	described below) and
		invention) include assays	immunodeficiencies (e.g., as
		disclosed in Miraglia et al., J	described below). Preferred
	-	Biomolecular Screening 4:193-	indications also include
		204(1999); Rowland et al.,	anemia, pancytopenia,
		"Lymphocytes: a practical	leukopenia, thrombocytopenia,
-		approach" Chapter 6:138-160	Hodgkin's disease, acute
		(2000); Satthaporn and	lymphocytic anemia (ALL),

plasmacytomas, multiple myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis (bacterial and	viral), Lyme Disease, asthma,	and allergy Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,
Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and	Verhasselt et al., J Immunol	158:2919-2925 (1997), the	contents of each of which are	herein incorporated by	reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.												
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	-					-																							
																							-1						

					metaplasia, and/or dysplasia.
	HLQDR48	1248	Production of TNF	TNFa FMAT. Assays for	A highly preferred
300			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred
				wide variety of inflammatory	embodiment of the invention
				and cytotoxic effects on a	includes a method for
				variety of cells are well known	stimulating (e.g., increasing)
				in the art and may be used or	TNF alpha production.
		-		routinely modified to assess	Highly preferred indications
				the ability of polypeptides of	include blood disorders (e.g.,
				the invention (including	as described below under
				antibodies and agonists or	"Immune Activity", "Blood-
		-		antagonists of the invention) to	Related Disorders", and/or
				mediate immunomodulation,	"Cardiovascular Disorders"),
				modulate inflammation and	Highly preferred indications
				cytotoxicity. Exemplary	include autoimmune diseases
				assays that test for	(e.g., rheumatoid arthritis,
				immunomodulatory proteins	systemic lupus erythematosis,
				evaluate the production of	Crohn"s disease, multiple
				cytokines such as tumor	sclerosis and/or as described
				necrosis factor alpha (TNFa),	below), immunodeficiencies
				and the induction or inhibition	(e.g., as described below),
				of an inflammatory or	boosting a T cell-mediated
				cytotoxic response. Such	immune response, and
				assays that may be used or	suppressing a T cell-mediated
				routinely modified to test	immune response. Additional
				immunomodulatory activity of	highly preferred indications
				polypeptides of the invention	include inflammation and

	(including antibodies and	inflammatory disorders, and
	agonists or antagonists of the	treating joint damage in
	invention) include assays	patients with rheumatoid
	disclosed in Miraglia et al., J	
	Biomolecular Screening 4:193-	- preferred indication is sepsis.
	204(1999); Rowland et al.,	Highly preferred indications
	"Lymphocytes: a practical	include neoplastic diseases
	approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
	(2000); Verhasselt et al., Eur J	
	Immunol 28(11):3886-3890	under "Hyperproliferative
	(1198); Dahlen et al., J	Disorders"). Additionally,
	Immunol 160(7):3585-3593	highly preferred indications
	(1998); Verhasselt et al., J	include neoplasms and
	Immunol 158:2919-2925	cancers, such as, leukemia,
	(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
	Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
	(1999), the contents of each of	
	which are herein incorporated	lung, colon, pancreatic,
	by reference in its entirety.	esophageal, stomach, brain,
	Human dendritic cells that may	
-	be used according to these	preferred indications include
	assays may be isolated using	benign dysproliferative
	techniques disclosed herein or	disorders and pre-neoplastic
	otherwise known in the art.	conditions, such as, for
	Human dendritic cells are	example, hyperplasia,
	antigen presenting cells in	metaplasia, and/or dysplasia.
	suspension culture, which,	Preferred indications include
	when activated by antigen	anemia, pancytopenia,
-	and/or cytokines, initiate and	leukopenia, thrombocytopenia,
	upregulate T cell proliferation	Hodgkin's disease, acute
	and functional activities.	lymphocytic anemia (ALL),

					plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
300	HLQDR48	1248	IL-8 in Normal Human Bronchial Epitheliae		
301	HLTAU74	1249	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection

	functions. Exemplary assays	(e.g., an infectious disease as
	for transcription through the	described below under
	AP1 response element that	"Infectious Disease"). Highly
	may be used or routinely	preferred indications include
	modified to test AP1-response	autoimmune diseases (e.g.,
	element activity of	rheumatoid arthritis, systemic
	polypeptides of the invention	lupus erythematosis, multiple
	(including antibodies and	sclerosis and/or as described
	agonists or antagonists of the	below) and
	invention) include assays	immunodeficiencies (e.g., as
-	disclosed in Berger et al., Gene	described below). Additional
	66:1-10 (1988); Cullen and	highly preferred indications
	Malm, Methods in Enzymol	include inflammation and
	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	272(49):30806-30811 (1997);	lymphoma, and/or as described
	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,
	reference in its entirety. T	lung, colon, pancreatic,
	cells that may be used	esophageal, stomach, brain,
	according to these assays are	liver, and urinary cancer. Other
	publicly available (e.g.,	preferred indications include
	through the ATCC).	benign dysproliferative
	Exemplary mouse T cells that	disorders and pre-neoplastic
	may be used according to these	conditions, such as, for

				assays include the CTLL cell	example, hyperplasia,
				dependent suspension-culture	Preferred indications include
				cell line with cytotoxic	arthritis, asthma, AIDS,
				activity.	allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
_					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HLTAU74	1249	Activation of	Kinase assay. Kinase assays,	A highly preferred
301	,		Natural Killer Cell	for example an Elk-1 kinase	embodiment of the invention
			ERK Signaling	assay, for ERK signal	includes a method for
	,		Pathway.	transduction that regulate cell	stimulating natural killer cell
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
	-			may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting natural
		-		of polypeptides of the	killer cell proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a
اللهي والساعة		-		the invention) to promote or	method for stimulating natural
		•		inhibit cell proliferation,	killer cell differentiation. An
)		activation, and differentiation.	alternative highly preferred

Exemplary assays for ERK	embodiment of the invention
 kinase activity that may be	includes a method for
used or routinely modified to	inhibiting natural killer cell
 test ERK kinase-induced	differentiation. Highly
activity of polypeptides of the	preferred indications include
invention (including antibodies	neoplastic diseases (e.g., as
 and agonists or antagonists of	described below under
the invention) include the	"Hyperproliferative
 assays disclosed in Forrer et	Disorders"), blood disorders
 al., Biol Chem 379(8-9):1101-	(e.g., as described below under
1110 (1998); Kyriakis JM,	"Immune Activity",
Biochem Soc Symp 64:29-48	"Cardiovascular Disorders",
(1999); Chang and Karin,	and/or "Blood-Related
Nature 410(6824):37-40	Disorders"), immune disorders
(2001); and Cobb MH, Prog	(e.g., as described below under
 Biophys Mol Biol 71(3-4):479-	"Immune Activity") and
500 (1999); the contents of	infections (e.g., as described
each of which are herein	below under "Infectious
incorporated by reference in its	Disease"). Preferred
entirety. Natural killer cells	indications include blood
that may be used according to	disorders (e.g., as described
these assays are publicly	below under "Immune
available (e.g., through the	Activity", "Blood-Related
ATCC). Exemplary natural	Disorders", and/or
killer cells that may be used	"Cardiovascular Disorders").
according to these assays	Highly preferred indications
include the human natural	include autoimmune diseases
killer cell lines (for example,	(e.g., rheumatoid arthritis,
NK-YT cells which have	systemic lupus erythematosis,
cytolytic and cytotoxic	multiple sclerosis and/or as
activity) or primary NK cells.	described below) and

	HLTDV50	1250	IL-10 in Human T-		
302			cell 2B9		
	HLTDV50	1250	Production of	Assays for measuring	Preferred embodiments of the
302	-		ICAM-1	expression of ICAM-1 are	invention include using
				well-known in the art and may	polypeptides of the invention
				be used or routinely modified	(or antibodies, agonists, or
				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	Inflammation, Vascular
		•		invention) to regulate ICAM-1	Disease, Athereosclerosis,
				expression. Exemplary assays	Restenosis, and Stroke
				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
				disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281	
				(2001); and, Miyamoto K, et	
				al., Am J Pathol, 156(5):1733-	
				1739 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
				entirety. Cells that may be	
				used according to these assays	
				are publicly available (e.g.,	•
				through the ATCC) and/or	
				may be routinely generated.	
				Exemplary cells that may be	
				used according to these assays	
			•	include microvascular	
				endothelial cells (MVEC).	

	HLTE125	1251	Activation of	This reporter assay measures	Highly preferred indications
303			transcription	activation of the GATA-3	include allergy, asthma, and
•			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
_				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
10				antibodies and agonists or	Preferred indications include
				antagonists of the invention) to	autoimmune diseases (e.g.,
				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as
				assays for transcription	described below). Preferred
				through the GATA3 response	indications include neoplastic
				element that may be used or	diseases (e.g., leukemia,
•				routinely modified to test	lymphoma, melanoma,
·*				GATA3-response element	prostate, breast, lung, colon,
				activity of polypeptides of the	pancreatic, esophageal,
				invention (including antibodies	stomach, brain, liver, and
				and agonists or antagonists of	urinary tract cancers and/or as
				the invention) include assays	described below under

		disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign
		216:362-368 (1992); Henthorn	dysproliferative disorders and
		et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
		85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
	•	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
		Quant Biol 64:563-571 (1999);	Preferred indications include
,		Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
		J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
		(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
		Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
		Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
		14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
		contents of each of which are	lymphoma, arthritis, AIDS,
		herein incorporated by	granulomatous disease,
		reference in its entirety. Mast	inflammatory bowel disease,
		cells that may be used	sepsis, neutropenia,
		according to these assays are	neutrophilia, psoriasis,
		publicly available (e.g.,	suppression of immune
		through the ATCC).	reactions to transplanted
		Exemplary human mast cells	organs and tissues, hemophilia,
		that may be used according to	hypercoagulation, diabetes
		these assays include the HMC-	mellitus, endocarditis,
		1 cell line, which is an	meningitis, and Lyme Disease.
		immature human mast cell line	
		established from the peripheral	
		blood of a patient with mast	
		cell leukemia, and exhibits	
		many characteristics of	
		immature mast cells.	

	HLTE125	1251	Activation of	This reporter assay measures	Highly preferred indications
303			transcription	activation of the NFAT	include allergy, asthma, and
-			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
		•	immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
	-		as mast cells).	cells has been linked to	described below under
		·		cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
		-		Activated T cells (NFAT)	include blood disorders (e.g.,
		-		response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
		_		agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
		-		modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as
				immunomodulatory functions.	described below). Preferred
				Exemplary assays for	indications include neoplastic
				transcription through the	diseases (e.g., leukemia,
				NFAT response element that	lymphoma, melanoma,
				may be used or routinely	prostate, breast, lung, colon,
				modified to test NFAT-	pancreatic, esophageal,
				response element activity of	stomach, brain, liver, and
				polypeptides of the invention	urinary tract cancers and/or as
				(including antibodies and	described below under

		agonists or antagonists of the	"Hyperproliferative
	-	invention) include assays	Disorders"). Other preferred
		disclosed in Berger et al., Gene	indications include benign
		66:1-10 (1998); Cullen and	dysproliferative disorders and
		Malm, Methods in Enzymol	pre-neoplastic conditions, such
		216:362-368 (1992); Henthorn	as, for example, hyperplasia,
		et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
		85:6342-6346 (1988); De Boer	Preferred indications include
		et al., Int J Biochem Cell Biol	anemia, pancytopenia,
		31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
		et al., J Immunol	leukemias, Hodgkin's disease,
		165(12):7215-7223 (2000);	acute lymphocytic anemia
		Hutchinson and McCloskey, J	(ALL), plasmacytomas,
		Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
		16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
		al., J Exp Med 188:527-537	granulomatous disease,
		(1998), the contents of each of	inflammatory bowel disease,
		which are herein incorporated	sepsis, neutropenia,
	-	by reference in its entirety.	neutrophilia, psoriasis,
		Mast cells that may be used	suppression of immune
		according to these assays are	reactions to transplanted
		publicly available (e.g.,	organs and tissues, hemophilia,
		through the ATCC).	hypercoagulation, diabetes
	~	Exemplary human mast cells	mellitus, endocarditis,
		that may be used according to	meningitis, and Lyme Disease.
		these assays include the HMC-	
		1 cell line, which is an	
	·	immature human mast cell line	
		established from the peripheral	
		blood of a patient with mast	
		cell leukemia, and exhibits	

				many characteristics of	
303	HLTE125	1251	IL-6 in HUVEC	Initiatule Iliast Cells.	
	HLTEJ06	1252	Activation of	Assays for the activation of	A preferred embodiment of
304			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
_				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn's disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),
				Methods in Enzymol 216:362-	boosting a T cell-mediated
				368 (1992); Henthorn et al.,	immune response, and
				Proc Natl Acad Sci USA	suppressing a T cell-mediated

!), the include inflammation and	hich are inflammatory disorders, and	-	ety. T patients with rheumatoid		says are preferred indication is sepsis.	.g., Highly preferred indications	include neoplastic diseases	cells that (e.g., leukemia, lymphoma,		TLL cell under "Hyperproliferative		n culture highly preferred indications	oxic include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include
85:6342-6346 (1988); and Black et al. Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.														

					organia mondrandia
					ancima, pancytopema,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HLTFA64	1253	Production of	IFNgamma FMAT. IFNg	A highly preferred
305			IFNgamma using	plays a central role in the	embodiment of the invention
			Natural Killer cells	immune system and is	includes a method for
				considered to be a	stimulating the production of
		_		proinflammatory cytokine.	IFNg. An alternative highly
				IFNg promotes TH1 and	preferred embodiment of the
				inhibits TH2; promotes IgG2a	invention includes a method
				and inhibits IgE; induces	for inhibiting the production of
		,		macrophage activation; and	IFNg. Highly preferred

Assays for proteins producins producins produced by variety of in activities are helper cell by known in the used or rour assess the applypeptide (including a agonists or invention) to inflammato modulate T function, are humoral or immuniny. That test for immunomo evaluate the cytokines, and the cotokines, and the cotokines, and the cotokines.	increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 helper cell function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon	indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", "Hyperproliferative Disorders" (e.g. cancer/tumorigenesis) and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiency (e.g., as described below), boosting a T cell-mediated
 actival	activation of T cells. Such	suppressing a T cell-mediated
assays routin immu polype	assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention	immune response, boosting antibody-dependent immune responses, suppressing antibody-dependent immune
(inclu	(including antibodies and	responses, boosting innate

anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.		A highly preferred indication is allergy. Another highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-
recognize antibody bound on target cells, via NK Fc receptors, leading to cell- mediated cytotoxicity.		Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6
	Glucose Production in H4IIE	Activation of transcription through STAT6 response element in immune cells (such as T-cells).
	1254	1254
	HLTHG37	HLTHG37
	306	306

				are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infectiou (e.g., an infectious disease as described below under "Infectious
307	HLWAA17	1255	Regulation of transcription of Malic Enzyme in adipocytes	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal

	Malic enzyme is involved in	Disorders" section below).
	lipogenesisand its expression is	diabetic neuropathy, nerve
	stimulted by insulin. ME	disease and nerve damage
 	promoter contains two direct	(e.g., due to diabetic
 	repeat (DR1)- like elements	neuropathy), blood vessel
	MEp and MEd identified as	blockage, heart disease, stroke,
	putative PPAR response	impotence (e.g., due to diabetic
 	elements. ME promoter may	neuropathy or blood vessel
	also responds to AP1 and other	blockage), seizures, mental
	transcription factors.	confusion, drowsiness,
 	Exemplary assays that may be	nonketotic hyperglycemic-
	used or routinely modified to	hyperosmolar coma,
	test for regulation of	cardiovascular disease (e.g.,
	transcription of Malic Enzyme	heart disease, atherosclerosis,
	(in adipoocytes) by	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
-	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
 	invention) include assays	"Cardiovascular Disorders"
 	disclosed in: Streeper, R.S., et	section below), dyslipidemia,
	al., Mol Endocrinol,	endocrine disorders (as
	12(11):1778-91 (1998);	described in the "Endocrine
	Garcia-Jimenez, C., et al., Mol	Disorders" section below),
 	Endocrinol, 8(10):1361-9	neuropathy, vision impairment
	(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
	Biol Chem, 274(25):17997-	blindness), ulcers and impaired
	8004 (1999); Ijpenberg, A., et	wound healing, and infection
	al., J Biol Chem,	(e.g., infectious diseases and
	272(32):20108-20117 (1997);	disorders as described in the
	Berger, et al., Gene 66:1-10	"Infectious Diseases" section
	(1988); and, Cullen, B., et al.,	below, especially of the

				Methods in Enzymol.	urinary tract and skin), carpal
				contents of each of which is	duffilet syndronie and Dupuytren's contracture).
				herein incorporated by	An additional highly preferred
				reference in its entirety.	indication is obesity and/or
				Hepatocytes that may be used	complications associated with
				according to these assays are	obesity. Additional highly
				publicly available (e.g.,	preferred indications include
				through the ATCC) and/or	weight loss or alternatively,
				may be routinely generated.	weight gain. Aditional
				Exemplary hepatocytes that	highly preferred indications are
				may be used according to these	complications associated with
				assays includes the H4IIE rat	insulin resistance.
				liver hepatoma cell line.	
	HLWAA17	1255	Production of	Assays for measuring	Preferred embodiments of the
			ICAM-1	expression of ICAM-1 are	invention include using
				well-known in the art and may	polypeptides of the invention
				be used or routinely modified	(or antibodies, agonists, or
				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	Inflammation, Vascular
				invention) to regulate ICAM-1	Disease, Athereosclerosis,
				expression. Exemplary assays	Restenosis, and Stroke
				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
_				disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281	
				(2001); and, Miyamoto K, et	
				al., Am J Pathol, 156(5):1733-	

	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention. A highly preferred embodiment of the invention
1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the
	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
	1256
	HLWAA88
	308

i	invention (including antibodies	includes a method for
 -	o atsingage or antagon be	otimilating anontonic of
 <u> </u>	and agomests of antagomests of	summaning apoptosis of
 · th	the invention) include the	endothelial cells. An
as	assays disclosed in Forrer et	alternative highly preferred
al	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
<u> </u>	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
 <u> </u>	Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
 [4	410(6824):37-40 (2001); and	includes a method for
 0	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
 B	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
ar	are herein incorporated by	embodiment of the invention
 re	reference in its entirety.	includes a method for
<u> </u>	Endothelial cells that may be	inhibiting (e.g., decreasing) the
 sn	used according to these assays	activation of and/or
ar	are publicly available (e.g.,	inactivating endothelial cells.
 th	through the ATCC).	A highly preferred
 <u> </u>	Exemplary endothelial cells	embodiment of the invention
 th	that may be used according to	includes a method for
- th	these assays include human	stimulating angiogenisis. An
m	umbilical vein endothelial cells	alternative highly preferred
(F	(HUVEC), which are	embodiment of the invention
 er	endothelial cells which line	includes a method for
 90	venous blood vessels, and are	inhibiting angiogenesis. A
ui	involved in functions that	highly preferred embodiment
ui	include, but are not limited to,	of the invention includes a
 ar	angiogenesis, vascular	method for reducing cardiac
pe	permeability, vascular tone,	hypertrophy. An alternative

highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include	neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive	heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular	disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under	"Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels
and immune cell extravasation.				
	,			

themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that	stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization.	Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s	sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi"s sarcoma, hemangioma (capillary and	cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma,	lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and
					-
	,				

urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury.
																					,								-	

		rheumatoid arthritis,
	,	cerebrovascular disease, renal
-		diseases such as acute renal
		failure, and osteoporosis.
		Additional highly preferred
		indications include stroke,
		graft rejection, diabetic or
		other retinopathies, thrombotic
		and coagulative disorders,
		vascularitis, lymph
		angiogenesis, sexual disorders,
		age-related macular
		degeneration, and treatment
		/prevention of endometriosis
		 and related conditions.
		Additional highly preferred
		indications include fibromas,
		heart disease, cardiac arrest,
		heart valve disease, and
		vascular disease.
		Preferred indications include
		blood disorders (e.g., as
		described below under
		 "Immune Activity", "Blood-
		Related Disorders", and/or
		"Cardiovascular Disorders").
		Preferred indications include
		autoimmune diseases (e.g.,
		rheumatoid arthritis, systemic
		 lupus erythematosis, multiple
		sclerosis and/or as described

below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cellmediate humor
	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1256
	HLWAA88
	308

chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line
																							-							

venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose eells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1257
	HLWAD77
	309

309	HLWAD77	1257	Activation of	3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety. Assays for the activation of transcription through the EGB	Preferred embodiments of the include using
308			transcription through the EGR (Early Growth Response) element in immune cells (such as B-cells).	transcription through the EGR response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate EGR transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the EGR response element that may be used or routinely modified to test EGR response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Autoimmunity, Allergy and Asthma.

ys Activity", "Blood-Related		"Cardiovascular Disorders"),			(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	1) Crohn"s disease, multiple		below), immunodeficiencies	(e.g., as described below),			suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	e inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	re preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	hat (e.g., leukemia, lymphoma,			Disorders"). Additionally,	re highly preferred indications		(
in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	
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		leukemia, lymphoma,
		melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		 disorders and pre-neoplastic
		conditions, such as, for
		 example, hyperplasia,
		metaplasia, and/or dysplasia.
	 	 Preferred indications include
		 anemia, pancytopenia,
		 leukopenia, thrombocytopenia,
		 Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		 plasmacytomas, multiple
		 myeloma, Burkitt's lymphoma,
		 arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
		 organs and tissues,
	 	 hemophilia, hypercoagulation,
		diabetes mellitus, endocarditis,
		meningitis, Lyme Disease,
		cardiac reperfusion injury, and

					asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
310	HLWAE11	1258	IL-10 in Human T-cell 2B9		
	HLWAE11	1258	Production of	Assays for measuring	Highly preferred indications
310			VCAM in	expression of VCAM are well-	include inflammation (acute
			endomental cens	Known in the art and may be	and enronic), restnosis,
		((such as numan	used of fournery modified to assess the ability of	allerov Hiohly preferred
			endothelial cells	polypeptides of the invention	indications include
			(HUVEC))	(including antibodies and	inflammation and
				agonists or antagonists of the	inflammatory disorders,
				invention) to regulate VCAM	immunological disorders,
				expression. For example,	neoplastic disorders (e.g.
				FMAT may be used to meaure	cancer/tumorigenesis), and
				the upregulation of cell surface	cardiovascular disorders (such
				VCAM-1 expresssion in	as described below under
				endothelial cells. Endothelial	"Immune Activity", "Blood-
				cells are cells that line blood	Related Disorders",
	·			vessels, and are involved in	"Hyperproliferative Disorders"
				functions that include, but are	and/or "Cardiovascular
				not limited to, angiogenesis,	Disorders"). Highly preferred
				vascular permeability, vascular	indications include neoplasms
				tone, and immune cell	and cancers such as, for
				extravasation. Exemplary	example, leukemia, lymphoma,
				endothelial cells that may be	melanoma, renal cell
				used according to these assays	carcinoma, and prostate,
				include human umbilical vein	breast, lung, colon, pancreatic,

	·		endothelial cells (HUVEC), which are available from commercial sources. The expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
HLWAE11	1258	Activation of transcription through NFKB response element in immune cells (such	lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses. Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified	Highly preferred indications include inflammatory disorders. Highly preferred indications include blood disorders (e.g.,
		as natural killer cells).	to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that	as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as

described below). An	additional highly preferred	indication is infection (e.g.,	AIDS, and/or an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	nder	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute
describe	addition	indicatio	AIDS, a	disease	under "I	Highly F		(e.g., me	lymphor				indicatio	and canc	example	carcinon	lymphor		esophage	liver and	preferre	benign d	disorder	condition	example	metaplas	Preferre	include 8	leukopei	
may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	NK cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human NK cells	that may be used according to	these assays include the NKL	cell line, which is a human	natural killer cell line	established from the peripheral
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					··	 -			 -																					
																			7.											

twith large lymphocytic anemia (ALL), plasmacytomas, multiple LL-2 dependent myeloma, Burkitt's lymphoma, re cell line has arthritis, AIDS, granulomatous sembling that disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.		uring calcium Preferred embodiments of the invention include using polypeptides of the invention ss the ability or routinely polypeptides of the invention of the antagonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of mobilize prevention, Inflammation, Atherosclerosis, trations of trations of trations of trations of tron of tion of ve signaling
blood of a patient with large granular lymphocytic leukemia. This IL-2 dependent suspension culture cell line has a morphology resembling that of activated NK cells.		Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling
	IL-8 in SW480	Calcium flux in immune cells (such as monocytes)
	1258	1258
,	HLWAE11	HLWAE11
	310	310

	A highly preferred embodiment of the invention includes a method for	stimulating (e.g., increasing)
pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux in immune cells (such as monocytes) include assays disclosed in: Chan, CC, et al., J Pharmacol Exp Ther, 269(3):891-896 (1994); Andersson, K, et al., Cytokine, 12(12):1784-1787 (2000); Scully, SP, et al., J Clin Invest, 74(2) 589-599 (1984); and, Sullivan, E, et al., Methods Mol Biol, 114:125-133 (1999), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the THP-1 monocyte cell line.	or ins ge	variety of cells and act to
	Production of MCP-1	
	1259	
	HLWA022	
	311	

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MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for	inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infections	disease as described below under "Infectious Disease").	indications include inflammation and	inflammatory disorders. Preferred indications include	blood disorders (e.g., as described below under	"Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"). Highly preferred indications	include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis, multiple sclerosis and/or as	described below) and immunodeficiencies (e.g., as	described below). Preferred	indications also include anemia, pancytopenia,	leukopenia, thrombocytopenia,
induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely	modified to assess the ability of polypeptides of the invention (including antibodies and acconists or antaconists of	the invention) to mediate immunomodulation, induce chemotaxis, and modulate	immune cell activation. Exemplary assays that test for	immunomodulatory proteins evaluate the production of cell	surface markers, such as monocyte chemoattractant	protein (MCP), and the activation of monocytes and T	cells. Such assays that may be used or routinely modified to	test immunomodulatory and differentiation activity of	polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays	disclosed in Miraglia et al., J	204(1999); Rowland et al.,	"Lymphocytes: a practical
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		,											

approach" Chapter 6:138-160 Hodgkin's disease, acute		Eremin, J R Coll Surg Ednb plasmacytomas, multiple		Verhasselt et al., J Immunol arthritis, AIDS, granulomatous		contents of each of which are disease, sepsis, neutropenia,	herein incorporated by neutrophilia, psoriasis,	reference in its entirety.	Human dendritic cells that may reactions to transplanted	be used according to these organs and tissues,	assays may be isolated using hemophilia, hypercoagulation,	techniques disclosed herein or diabetes mellitus, endocarditis,	otherwise known in the art. meningitis (bacterial and	Human dendritic cells are viral), Lyme Disease, asthma,	antigen presenting cells in and allergy Preferred			and/or cytokines, initiate and leukemia, lymphoma, and/or as	upregulate T cell proliferation described below under	and functional activities. "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neonlastic
approac	(2000);	Eremin	45(1):9	Verhass	158:291	content	herein	reference	Human	pe nsed	assays I	techniq	otherwi	Human	antigen	suadsns	when ac	and/or c	nbregul	and fun										-

					conditions, such as, for example, hyperplasia,
311	HLWA022	1259	IL-10 in Human T-cell 2B9		metapiasia, and/or dyspiasia.
	HLWA022	1259	Activation of	Assays for the activation of	Highly preferred indications
311		-	transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response in immune	cells (NFAT) response element	"Immune Activity", "Blood-
_			cells (such as T-	are well-known in the art and	Related Disorders", and/or
			cells).	may be used or routinely	"Cardiovascular Disorders").
				modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An
				polypeptides of the invention	additional highly preferred
				(including antibodies and	indication is infection (e.g., an
				agonists or antagonists of the	infectious disease as described
				invention) include assays	below under "Infectious
				disclosed in Berger et al., Gene	Disease"). Preferred

	66:1-10 (1998); Cullen and	indications include neoplastic
 	Malm, Methods in Enzymol	diseases (e.g., leukemia,
	216:362-368 (1992); Henthorn	lymphoma, and/or as described
	et al., Proc Natl Acad Sci USA	below under
 	85:6342-6346 (1988); Serfling	"Hyperproliferative
	et al., Biochim Biophys Acta	Disorders"). Preferred
 	1498(1):1-18 (2000); De Boer	indications include neoplasms
 	et al., Int J Biochem Cell Biol	and cancers, such as, for
	31(10):1221-1236 (1999);	example, leukemia, lymphoma,
 9	Fraser et al., Eur J Immunol	and prostate, breast, lung,
	29(3):838-844 (1999); and	colon, pancreatic, esophageal,
 	Yeseen et al., J Biol Chem	stomach, brain, liver and
	268(19):14285-14293 (1993),	urinary cancer. Other preferred
	the contents of each of which	indications include benign
 	are herein incorporated by	dysproliferative disorders and
	reference in its entirety. T	pre-neoplastic conditions, such
 	cells that may be used	as, for example, hyperplasia,
 	according to these assays are	metaplasia, and/or dysplasia.
	publicly available (e.g.,	Preferred indications also
-	through the ATCC).	include anemia, pancytopenia,
 	Exemplary human T cells that	leukopenia, thrombocytopenia,
-	may be used according to these	Hodgkin's disease, acute
	assays include the JURKAT	lymphocytic anemia (ALL),
 	cell line, which is a suspension	plasmacytomas, multiple
	culture of leukemia cells that	myeloma, Burkitt's lymphoma,
	produce IL-2 when stimulated.	arthritis, AIDS, granulomatous
 		disease, inflammatory bowel
 		disease, sepsis, neutropenia,
 		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted

					organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
	HLWA022	1259	Activation of	Assays for the activation of	A preferred embodiment of
311			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
_			cells).	the ability of polypeptides of	of the invention includes a
	-			the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and

suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and	inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly	preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below	under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and	leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esonhageal, stomach, brain	liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of	which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g.,	through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer	cell line with cytolytic and cytotoxic activity.	

					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HLWAY54	1260	Production of	MCP-1 FMAT. Assays for	A highly preferred
312			MCP-1	immunomodulatory proteins	embodiment of the invention
				that are produced by a large	includes a method for
				variety of cells and act to	stimulating (e.g., increasing)
·				induce chemotaxis and	MCP-1 production. An
				activation of monocytes and T	alternative highly preferred
				cells are well known in the art	embodiment of the invention
				and may be used or routinely	includes a method for

				Verhasselt et al., J Immunol	arthritis. AIDS, granulomatous
				158:2919-2925 (1997), the	disease, inflammatory bowel
				contents of each of which are	disease, sepsis, neutropenia,
				herein incorporated by	neutrophilia, psoriasis,
				reference in its entirety.	suppression of immune
				Human dendritic cells that may	reactions to transplanted
				be used according to these	organs and tissues,
				assays may be isolated using	hemophilia, hypercoagulation,
				techniques disclosed herein or	diabetes mellitus, endocarditis,
				otherwise known in the art.	meningitis (bacterial and
				Human dendritic cells are	viral), Lyme Disease, asthma,
				antigen presenting cells in	and allergy Preferred
				suspension culture, which,	indications also include
				when activated by antigen	neoplastic diseases (e.g.,
				and/or cytokines, initiate and	leukemia, lymphoma, and/or as
				upregulate T cell proliferation	described below under
				and functional activities.	"Hyperproliferative
					Disorders"). Highly preferred
					indications include neoplasms
					and cancers, such as, leukemia,
					lymphoma, prostate, breast,
					lung, colon, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
	L				metaplasia, and/or dysplasia.
I	HLWAY54	1260	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications

312	Signaling Pathway	assays for signal transduction	include asthma, allergy,
	 in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
	 (such as	activation, or apoptosis are	inflammation, and
	 eosinophils).	well known in the art and may	inflammatory disorders.
	 	be used or routinely modified	Additional highly preferred
	 	to assess the ability of	indications include immune
	 	polypeptides of the invention	and hematopoietic disorders
		(including antibodies and	(e.g., as described below under
		agonists or antagonists of the	"Immune Activity", and
	 	invention) to promote or	"Blood-Related Disorders"),
	 	inhibit cell proliferation,	autoimmune diseases (e.g.,
		activation, and apoptosis.	rheumatoid arthritis, systemic
		Exemplary assays for JNK	Iupus erythematosis, Crohn"s
		kinase activity that may be	disease, multiple sclerosis
	 -	used or routinely modified to	and/or as described below),
10	 	test JNK kinase-induced	immunodeficiencies (e.g., as
		activity of polypeptides of the	described below). Highly
		invention (including antibodies	preferred indications also
	 	and agonists or antagonists of	include boosting or inhibiting
		the invention) include the	immune cell proliferation.
		assays disclosed in Forrer et	Preferred indications include
		al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
		1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
		Cell Res 247(2): 495-504	described below under
	 	(1999); Kyriakis JM, Biochem	"Hyperproliferative
		Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
		Chang and Karin, Nature	indications include boosting an
	 	410(6824):37-40 (2001); and	eosinophil-mediated immune
		Cobb MH, Prog Biophys Mol	response, and suppressing an
		Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune
		the contents of each of which	response.

are herein incorporated by reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils. Fosinophils are important in	the late stage of allergic	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);
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				Hebestreit H. et al	
				"Disruption of fas receptor	
				signaling by nitric oxide in	
				eosinophils" J Exp Med; Feb	
				2;187(3):415-25 (1998); J	
				Allergy Clin Immunol 1999	, ,
				Sep;104(3 Pt 1):565-74; and,	
				Sousa AR, et al., "In vivo	
				resistance to corticosteroids in	
				bronchial asthma is associated	
				with enhanced	
				phosyphorylation of JUN N-	
				terminal kinase and failure of	
				prednisolone to inhibit JUN N-	
				terminal kinase	
				phosphorylation" J Allergy	
				Clin Immunol; Sep;104(3 Pt	
				1):565-74 (1999); the contents	
				of each of which are herein	
				incorporated by reference in its	
				entirety.	
	HLWAY54	1260	SEAP in		
312			HepG2/Squale-		
			synthetase(stimulati		
	HI WAVS4	10,00	CD150 in Human T		
312	+C1247111	1200	cells		
	HLWAY54	1260	SEAP in OE-33		
312					
	HLWAY54	1260	SEAP in		
312			Senescence Assay		

	HLWBH18	1261	Inhibition of	Reporter Assay: construct	
313			squalene synthetase	contains regulatory and coding	
			gene transcription.	sequence of squalene	
•				synthetase, the first specific	
-				enzyme in the cholesterol	
			-	biosynthetic pathway. See	
				Jiang, et al., J. Biol. Chem.	
				268:12818-128241(993), the	
	~~~			contents of which are herein	
				incorporated by reference in its	
				entirety. Cells were treated	
				with SID supernatants, and	
				SEAP activity was measured	
				after 72 hours. HepG2 is a	
				human hepatocellular	
				carcinoma cell line (ATCC	
				HB-8065). See Knowles et al.,	
				Science. 209:497-9 (1980), the	
				contents of which are herein	
				incorporated by reference in its	
	,			entirety.	
	HLWBH18	1261	Activation of	Kinase assay. JNK and p38	A highly preferred
313			Endothelial Cell	kinase assays for signal	embodiment of the invention
			p38 or JNK	transduction that regulate cell	includes a method for
	-		Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
				apoptosis are well known in	growth. An alternative highly
···				the art and may be used or	preferred embodiment of the
				routinely modified to assess	invention includes a method
				the ability of polypeptides of	for inhibiting endothelial cell
				the invention (including	growth. A highly preferred
				antibodies and agonists or	embodiment of the invention

antagonists of the invention) to promote or inhibit cell proliferation, activation, and apptosis. Exemplary assays proliferation, activation, and apptosis. Exemplary assays discipled to test INK and p38 kinase activity that may be used or method for inhibiting routinely modified to test INK and p38 kinase activity that may be used or method for inhibiting and politicely modified to test INK and p38 kinase-induced activity of polypeptides of the invention included the analysis of antagonisis of antagonisis of the invention include the assays disclosed in Forence at al., Biol Chem 379(8-29):1101- al. Biol Chem 370(8-29):1101- al. Biol Chem 370(8-29): al. Biol Chem 370(8-29):1101- al. Biol Chem 370(8-29): al. Biol Chem 370(8-29):1101- al. Biol Chem
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stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for	inhibiting angiogenesis. A highly preferred embodiment of the invention includes a	method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a	method for inducing cardiac hypertrophy. Highly preferred indications include	neoplastic diseases (e.g., as described below under	"Hyperproliferative Disorders"), and disorders of the cardiovascular system	(e.g., heart disease, congestive heart failure, hypertension,	aortic stenosis, cardiomyopathy, valvular	regurgitation, left ventricular dysfunction, atherosclerosis	and atherosclerotic vascular disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or
these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line	venous blood vessels, and are involved in functions that include, but are not limited to,	angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.										

as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi's sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,
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angiosarcoma, haemangiopericytoma, lymphangiosarcoma. Highly	preserved indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s	disease and Reynaud"s phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly

preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as
	-														-															
		-							-	-									-											
																				-										

					described below under
					"Immune Activity", "Blood-
					Related Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
		~			preferred indications include
-					inflammation and
					inflammatory disorders (such
					as acute and chronic
,					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
313	HLWBH18	1261	SEAP in OE-33		
314	HLWBI63	1262	CD71 in Human T cells		
	HLWBK05	1263	Activation of	Kinase assay. Kinase assays,	A highly preferred
315			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a

method for inhibiting	adipocyte proliferation. A	highly preferred embodiment	of the invention includes a	method for stimulating	adipocyte differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting adipocyte	differentiation. A highly	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	("Hyperproliferative
modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	(107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that
					~	<u> </u>				44						-														

			may be made according to these	Diggidanci) Drofomod
			may be used according to mese	indications include blood
	_	 -	assays are publicly available	indications include olood
_			(e.g., through the ATCC).	disorders (e.g., hypertension,
			Exemplary mouse adipocyte	congestive heart failure, blood
			cells that may be used	vessel blockage, heart disease,
			according to these assays	stroke, impotence and/or as
		 	include 3T3-L1 cells. 3T3-L1	described below under
			is an adherent mouse	"Immune Activity",
			preadipocyte cell line that is a	"Cardiovascular Disorders",
			continuous substrain of 3T3	and/or "Blood-Related
-77			fibroblast cells developed	Disorders"), immune disorders
			through clonal isolation and	(e.g., as described below under
			undergo a pre-adipocyte to	"Immune Activity"), neural
			adipose-like conversion under	disorders (e.g., as described
			appropriate differentiation	below under "Neural Activity
	-		conditions known in the art.	and Neurological Diseases"),
				and infection (e.g., as
				described below under
				"Infectious Disease").
-				A highly preferred indication
				is diabetes mellitus. An
				additional highly preferred
				indication is a complication
				associated with diabetes (e.g.,
				diabetic retinopathy, diabetic
				nephropathy, kidney disease
				(e.g., renal failure,
				nephropathy and/or other
				diseases and disorders as
				described in the "Renal
· · · · · ·				Disorders" section below),

diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke,	impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness,	nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g.,	microvascular disease, hypertension, stroke, and other diseases and disorders as	described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine	Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired	wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An
					29	
		•				

additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include	weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with	Additional highly preferred indications are disorders of the musculoskeletal systems	including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include.	hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia.	and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as,	breast, colon, and kidney cancer. Additional preferred indications include melanoma,
			-			

					prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
316	HLWBY76	1264	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,

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Crohn"s disease, multiple sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other
antagonists of the invention) include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.							
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			preferre benign ( disorder conditic example metapla Preferre anemia, leukope Hodgki lympho plasmac myelom arthritis disease, neutropl suppress reaction organs a hemoph diabetes meningi cardiac asthma addition is infect	preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e. o. an infectious
			disease	disease as described below
HLWBY76 126	1264	CD152 in Human T	under "	under "Intectious Disease").

	HI WBV76	1264	HI A-DR in Hilman		
316			T cells		
	HLWCF05	1265	Activation of	Kinase assay. Kinase assays,	A highly preferred
317			Adipocyte PI3	for example an GSK-3 assays,	embodiment of the invention
			Kinase Signalling	for PI3 kinase signal	includes a method for
			Pathway	transduction that regulate	increasing adipocyte survival
				glucose metabolism and cell	An alternative highly preferred
				survival are well-known in the	embodiment of the invention
		,,		art and may be used or	includes a method for
				routinely modified to assess	decreasing adipocyte survival.
				the ability of polypeptides of	A preferred embodiment of the
				the invention (including	invention includes a method
				antibodies and agonists or	for stimulating adipocyte
				antagonists of the invention) to	proliferation. An alternative
				promote or inhibit glucose	highly preferred embodiment
,				metabolism and cell survival.	of the invention includes a
				Exemplary assays for PI3	method for inhibiting
				kinase activity that may be	adipocyte proliferation. A
				used or routinely modified to	preferred embodiment of the
-				test PI3 kinase-induced activity	invention includes a method
				of polypeptides of the	for stimulating adipocyte
				invention (including antibodies	differentiation. An alternative
				and agonists or antagonists of	highly preferred embodiment
				the invention) include assays	of the invention includes a
				disclosed in Forrer et al., Biol	method for inhibiting
				Chem 379(8-9):1101-1110	adipocyte differentiation.
				(1998); Nikoulina et al.,	Highly preferred indications
				Diabetes 49(2):263-271	include endocrine disorders
				(2000); and Schreyer et al.,	(e.g., as described below under
				Diabetes 48(8):1662-1666	"Endocrine Disorders").
				(1999), the contents of each of	Preferred indications include

			which are herein incorporated	neoplastic diseases (e.g
			hy reference in its entirety	linomos linosomos ond/or
			by reference in its entirety.	Ilpollias, liposalcollias, allo, of
		٠	Mouse adipocyte cells that	as described below under
	••		may be used according to these	"Hyperproliferative
			assays are publicly available	Disorders"), blood disorders
-			(e.g., through the ATCC).	(e.g., hypertension, congestive
	,		Exemplary mouse adipocyte	heart failure, blood vessel
			cells that may be used	blockage, heart disease, stroke,
			according to these assays	impotence and/or as described
			include 3T3-L1 cells. 3T3-L1	below under "Immune
			is an adherent mouse	Activity", "Cardiovascular
			preadipocyte cell line that is a	Disorders", and/or "Blood-
			continous substrain of 3T3	Related Disorders"), immune
			fibroblast cells developed	disorders (e.g., as described
			through clonal isolation and	below under "Immune
			undergo a pre-adipocyte to	Activity"), neural disorders
			adipose-like conversion under	(e.g., as described below under
			appropriate differentiation	"Neural Activity and
			conditions known in the art.	Neurological Diseases"), and
				infection (e.g., as described
				below under "Infectious
				Disease"). A highly
				preferred indication is diabetes
				mellitus. An additional
				highly preferred indication is a
				complication associated with
				diabetes (e.g., diabetic
				retinopathy, diabetic
				nephropathy, kidney disease
		_		(e.g., renal failure,
				nephropathy and/or other

"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Highly preferred	indications include neoplasms
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														-										-						

					and cancer, such as, lipoma, liposarcoma, lymphoma,
					leukemia and breast, colon,
					and kidney cancer. Additional
			,		highly preferred indications
					include melanoma, prostate,
					lung, pancreatic, esophageal,
-					stomach, brain, liver, and
					urinary cancer. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
	HLWCF05	1265	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
317	-		Signaling Pathway	assays for signal transduction	include asthma, allergy,
_			in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			(such as	activation, or apoptosis are	inflammation, and
			eosinophils).	well known in the art and may	inflammatory disorders.
				be used or routinely modified	Additional highly preferred
				to assess the ability of	indications include immune
				polypeptides of the invention	and hematopoietic disorders
				(including antibodies and	(e.g., as described below under
				agonists or antagonists of the	"Immune Activity", and
·				invention) to promote or	"Blood-Related Disorders"),
				inhibit cell proliferation,	autoimmune diseases (e.g.,
				activation, and apoptosis.	rheumatoid arthritis, systemic
				Exemplary assays for JNK	lupus erythematosis, Crohn"s
				kinase activity that may be	disease, multiple sclerosis
		-		used or routinely modified to	and/or as described below),
		-		test JNK kinase-induced	immunodeficiencies (e.g., as

activity of polypeptides of the	described below). Highly
invention (including antibodies	preferred indications also
and agonists or antagonists of	include boosting or inhibiting
the invention) include the	immune cell proliferation.
assays disclosed in Forrer et	Preferred indications include
al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
Cell Res 247(2): 495-504	described below under
(1999); Kyriakis JM, Biochem	"Hyperproliferative
Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
Chang and Karin, Nature	indications include boosting an
410(6824):37-40 (2001); and	eosinophil-mediated immune
Cobb MH, Prog Biophys Mol	response, and suppressing an
Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune
the contents of each of which	response.
are herein incorporated by	
reference in its entirety.	
Exemplary cells that may be	
used according to these assays	
include eosinophils.	
Eosinophils are important in	
the late stage of allergic	
reactions; they are recruited to	
tissues and mediate the	
inflammatory response of late	
stage allergic reaction.	
Moreover, exemplary assays	
that may be used or routinely	
modified to assess the ability	
of polypeptides of the	
invention (including antibodies	:

and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep:104(3 Pt 1):565-74; and,	In vivo	sociated	N- e of	ż	
and agonists or antagoni; the invention) to modula signal transduction, cell proliferation, activation, apoptosis in eosinophils include assays disclosed cited in: Zhang JP, et al., of caspases in dexametha induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protei kinase in human eosinop Clin Exp Immunol; Oct; 122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas recept signaling by nitric oxide eosinophils" J Exp Med; 2;187(3):415-25 (1998); Allergy Clin Immunol 19 Sep;104(3 Pt 1):565-74;	Sousa AR, et al., "In vivo resistance to corticosteroids in	bronchial asthma is associated with enhanced	phosyphorylation of JUN N-terminal kinase and failure of	prednisolone to inhibit JUN N-	terminal kinase

				Clin Immunol: Sep. 104/3 Pt	
				1):565-74 (1999); the contents of each of which are herein	
				incorporated by reference in its entirety.	
317	HLWCF05	1265	SEAP in OE-21		
317	HLWCF05	1265	SEAP in OE-33		
	HLWCF05	1265	Activation of	Assays for the activation of	Preferred indications
317			transcription	transcription through the AP1	include neoplastic diseases
			through AP1	response element are well-	(e.g., as described below under
			response element in	known in the art and may be	"Hyperproliferative
			immune cells (such	used or routinely modified to	Disorders"), blood disorders
			as T-cells).	assess the ability of	(e.g., as described below under
				polypeptides of the invention	"Immune Activity",
<u>.                                    </u>				(including antibodies and	"Cardiovascular Disorders",
				agonists or antagonists of the	and/or "Blood-Related
				invention) to modulate growth	Disorders"), and infection
				and other cell functions.	(e.g., an infectious disease as
				Exemplary assays for	described below under
				transcription through the AP1	"Infectious Disease"). Highly
				response element that may be	preferred indications include
				used or routinely modified to	autoimmune diseases (e.g.,
				test AP1-response element	rheumatoid arthritis, systemic
				activity of polypeptides of the	lupus erythematosis, multiple
	-			invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below) and
		•		the invention) include assays	immunodeficiencies (e.g., as
				disclosed in Berger et al., Gene	described below). Additional
				66:1-10 (1988); Cullen and	highly preferred indications

include inflammation and inflammatory disorders. Highly preferred indications	also include neoplastic diseases (e.g., leukemia,	lymphoma, and/or as described below under	"Hyperproliferative Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	arthritis, asthma, AIDS,	allergy, anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	granulomatous disease,	inflammatory bowel disease.
Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Rellahan et al., J Biol Chem	272(49):30800-30811 (1997); Chang et al., Mol Cell Biol	18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol	29(3):838-844 (1999), the	contents of each of which are	reference in its entirety.	Human T cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is an IL-2 and IL-4	responsive suspension-culture	cell line.								
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sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	
	Activation of transcription through the CD28 response element are well-response element are well-response element are well-response element in known in the art and may be immune cells (such assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells.  Exemplary assays for transcription through the CD28 response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA
	HLWCF05 1265
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Additional highly preferred indications include inflammation and	inflammatory disorders. Highly preferred indications	include autoimmune diseases (e.g., rheumatoid arthritis.	systemic lupus erythematosis,	multiple scierosis and/or as described below),	immunodeficiencies (e.g., as	described below), boosting a T	response and compressing a T	cell-mediated immune	response. Highly preferred	indications include neoplastic	diseases (e.g., melanoma, renal	cell carcinoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma (e.g.,	metastatic melanoma), renal	cell carcinoma (e.g., metastatic	renal cell carcinoma),	leukemia, lymphoma (e.g., T	cell lymphoma), and prostate
McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997): Parra et al J Imminol	166(4):2437-2443 (2001); and Butscher et al., J Biol Chem	3(1):552-560 (1998), the contents of each of which are	herein incorporated by	cells that may be used	according to these assays are	publicly available (e.g.,	unough the $AICC$ ).	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.												
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breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for
metaplasia, and/or dysplasia. A highly preferred indication includes infection (e.g., AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below index "Infectious Disease.")
highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis,
psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").

					include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes melitus, endocarditis, meningitis, Lyme Disease, asthma and alleroy
317	HL WCF05	1265	Activation of transcription through NFAT response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T

response. Additional highly	preferred indications include	inflammation and	inflammatory disorders. An	additional highly preferred	indication is infection (e.g., an	infectious disease as described	below under "Infectious	Disease"). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	and prostate, breast, lung,	colon, pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute
NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Serfling	et al., Biochim Biophys Acta	1498(1):1-18 (2000); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these
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additional highly preferred indication is infection (e.g.,	AIDS, and/or an infectious disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such	as,melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL).
modified to test NFKB-response element activity of	polypeptides of the invention   (including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Gnes 15(2):105-117	(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.			
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					plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted
318	HLYAC95	1266	Glucose Production in H4IIE		organic, admina and and E.J.
318	nr 19093	000	Froduction of IFNgamma using a T cells	a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"),

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losis,	ed with	tosns	ant	r as	ıder	e"). Higł	ns incluc	e (e.g.,	s, systen	s, multip	describe	ficiency	below),	ediated	and	Il-media	Additio	dication	on and	ders.	Ę,	idiopatl	. High	ns incluc	(e.g.,	na,	as descri		4)	y prefen
tubercu	associate	ınuloma	l malign	is, and/c	selow ur	Disease	ndicatio	ne diseas	l arthriti	ematosi	nd/or as	munode	scribed	T cell-n	sponse,	g a T cel	sponse.	erred in	lammati	ory disor	preferre	include	fibrosis	ndicatio	diseases	lymphor	, and/or	er	liferativ	). Highl
infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred
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nd may	modified	JC	e invent	lies and	nists of	iate	on, regul	vities,	lper cell	nediate	ediated	olary ass		ry protei	ction of	Interfer	nd the	lls. Such	ю pəsn ə	d to test	ry activi	e invent	lies and	nists of	the ass	glia et al	eening 4	and et al	practical	r 6:138-
the art a	outinely	ability o	des of th	g antiboc	or antago	) to med	nodulatie	itory acti	TH2 he	and/or n	or cell-m	'. Exem	or	nodulato	the produ	s, such as	FNg), an	of T ce	at may b	modifie	nodulato	des of th	g antiboc	or antago	) include	in Mira	ular Scr	9); Rowl	cytes: a	" Chapte
known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160
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indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate,	breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benign dysproliferative	conditions, such as, for example, hyperplasia.	metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia, Hodgkin's disease, acute	lymphocytic anemia (ALL),	prasmacytomas, mumpie myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous disease inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted organs and tissues	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease, asthma and allergy.
(2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm	et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford)	38(3):214-20 (1999), the contents of each of which are berein incomparated by	reference in its entirety.  Human T cells that may be	used according to these assays may be isolated using	techniques disclosed herein or	otherwise known in the art. Human T cells are primary	human lymphocytes that	express a T Cell receptor and	CD3, CD4, or CD8. These cells mediate humoral or cell-	mediated immunity and may	be preactivated to enhance	responsiveness to	minimization and the second seconds.			
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A highly preferred	indication is diabetes mellitus.	An additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,
Assays for measuring secretion	of insulin are well-known in	the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	stimulate insulin secretion.	For example, insulin secretion	is measured by FMAT using	anti-rat insulin antibodies.	Insulin secretion from	pancreatic beta cells is	upregulated by glucose and	also by certain	proteins/peptides, and	disregulation is a key	component in diabetes.	Exemplary assays that may be	used or routinely modified to	test for stimulation of insulin	secretion (from pancreatic	cells) by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Ahren, B., et al.,	Am J Physiol, 277(4 Pt	2):R959-66 (1999); Li, M., et	al., Endocrinology,
Stimulation of	from percetion	Iroin pancreauc	beta cells.																									-		
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HLYAC95																														
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				138(9):3735-40 (1997); Kim.	endocrine disorders (as
				K.H. et al FFBS Lett	described in the "Endocrine
				377(2):237 0 (1005): cmd	Canadam's action 1-1-1-1
				311(2):231-9 (1993); and,	Disorders section below),
				Miraglia S et. al., Journal of	neuropathy, vision impairment
				Biomolecular Screening,	(e.g., diabetic retinopathy and
				4:193-204 (1999), the contents	blindness), ulcers and impaired
_				of each of which is herein	wound healing, and infection
				incorporated by reference in its	(e.g., infectious diseases and
				entirety. Pancreatic cells that	disorders as described in the
				may be used according to these	"Infectious Diseases" section
				assays are publicly available	below, especially of the
				(e.g., through the ATCC)	urinary tract and skin), carpal
				and/or may be routinely	tunnel syndrome and
-				generated. Exemplary	Dupuytren's contracture).
				pancreatic cells that may be	An additional highly preferred
				used according to these assays	indication is obesity and/or
				include rat INS-1 cells. INS-1	complications associated with
				cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
				These cells retain	highly preferred indications are
				characteristics typical of native	complications associated with
				pancreatic beta cells including	insulin resistance.
		-		glucose inducible insulin	
				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	
318	HLYAC95	1266	Hexosaminidase in RBL -2H3		
	HLYAF80	1267	SEAP in		

	1		NK16/STAT6		
HLYAN59	N59	1268	CD152 in Human T		
HLYAN59	N59	1268	HLA-DR in Human T cells	,	
HLYAN59	N59	1268	Production of	Assays for measuring	Highly preferred indications
			VCAM in	expression of VCAM are well-	include inflammation (acute
			endothelial cells	known in the art and may be	and chronic), restnosis,
			(such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
			endothelial cells	polypeptides of the invention	indications include
			(HUVEC))	(including antibodies and	inflammation and
				agonists or antagonists of the	inflammatory disorders,
				invention) to regulate VCAM	immunological disorders,
				expression. For example,	neoplastic disorders (e.g.
				FMAT may be used to meaure	cancer/tumorigenesis), and
				the upregulation of cell surface	cardiovascular disorders (such
				VCAM-1 expresssion in	as described below under
				endothelial cells. Endothelial	"Immune Activity", "Blood-
				cells are cells that line blood	Related Disorders",
				vessels, and are involved in	"Hyperproliferative Disorders"
				functions that include, but are	and/or "Cardiovascular
				not limited to, angiogenesis,	Disorders"). Highly preferred
	•			vascular permeability, vascular	indications include neoplasms
				tone, and immune cell	and cancers such as, for
				extravasation. Exemplary	example, leukemia, lymphoma,
				endothelial cells that may be	melanoma, renal cell
				used according to these assays	carcinoma, and prostate,
				include human umbilical vein	breast, lung, colon, pancreatic,
	-		-	endothelial cells (HUVEC),	esophageal, stomach, brain,
i				which are available from	liver and urinary cancer. Other

			`	commercial sources. The expression of VCAM (CD106), a membraneassociated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses	preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
321	HLYAP91	1769	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte

	activity of polypeptides of the	preferred embodiment of the
<u>.                                    </u>	invention (including antibodies	
	and agonists or antagonists of	for stimulating (e.g.,
	the invention) include the	increasing) adipocyte
	assays disclosed in Forrer et	activation. An alternative
	al., Biol Chem 379(8-9):1101-	highly preferred embodiment
	1110 (1998); Le Marchand-	of the invention includes a
	Brustel Y, Exp Clin	method for inhibiting the
<u></u>	Endocrinol Diabetes	activation of (e.g., decreasing)
	107(2):126-132 (1999);	and/or inactivating adipocytes.
	Kyriakis JM, Biochem Soc	Highly preferred indications
	Symp 64:29-48 (1999); Chang	include endocrine disorders
	and Karin, Nature	(e.g., as described below under
7	410(6824):37-40 (2001); and	"Endocrine Disorders").
	Cobb MH, Prog Biophys Mol	Highly preferred indications
	Biol 71(3-4):479-500 (1999);	also include neoplastic
	the contents of each of which	diseases (e.g., lipomas,
	are herein incorporated by	liposarcomas, and/or as
1	reference in its entirety.	described below under
	Mouse adipocyte cells that	"Hyperproliferative
I	may be used according to these	
	assays are publicly available	indications include blood
	(e.g., through the ATCC).	disorders (e.g., hypertension,
	Exemplary mouse adipocyte	congestive heart failure, blood
	cells that may be used	vessel blockage, heart disease,
	according to these assays	stroke, impotence and/or as
• <b>•</b>	include 3T3-L1 cells. 3T3-L1	described below under
<u>. 1</u>	is an adherent mouse	'"Immune Activity",
	preadipocyte cell line that is a	"Cardiovascular Disorders",
	continuous substrain of 3T3	and/or "Blood-Related
I	fibroblast cells developed	Disorders"), immune disorders

(e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases")	and infection (e.g., as described below under "Infectious Disease").	A highly preferred indication is diabetes mellitus.  An additional highly preferred indication is a complication.	associated with diabetes (e.g., diabetic retinopathy, diabetic	nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other	diseases and disorders as described in the "Renal Disorders" section below),	diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic	neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic	neuropathy or blood vessel blockage), seizures, mental	nonketotic hyperglycemichyperosmolar coma.
through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.			,						
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cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease,	hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders"	section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below),	neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infection 1	disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred	indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively,	weight gain. Additional highly preferred indications are complications associated with insulin resistance.  Additional highly preferred
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indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate lung pancreatic
esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.

	HLYAZ61	1270	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
322			Signaling Pathway	assays for signal transduction	include asthma, allergy,
			in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			(such as	activation, or apoptosis are	inflammation, and
			eosinophils).	well known in the art and may	inflammatory disorders.
				be used or routinely modified	Additional highly preferred
				to assess the ability of	indications include immune
				polypeptides of the invention	and hematopoietic disorders
		. 41		(including antibodies and	(e.g., as described below under
				agonists or antagonists of the	"Immune Activity", and
				invention) to promote or	"Blood-Related Disorders"),
				inhibit cell proliferation,	autoimmune diseases (e.g.,
				activation, and apoptosis.	rheumatoid arthritis, systemic
				Exemplary assays for JNK	lupus erythematosis, Crohn"s
				kinase activity that may be	disease, multiple sclerosis
				used or routinely modified to	and/or as described below),
				test JNK kinase-induced	immunodeficiencies (e.g., as
				activity of polypeptides of the	described below). Highly
				invention (including antibodies	preferred indications also
			-	and agonists or antagonists of	include boosting or inhibiting
				the invention) include the	immune cell proliferation.
				assays disclosed in Forrer et	Preferred indications include
				al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
				1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
				Cell Res 247(2): 495-504	described below under
		•		(1999); Kyriakis JM, Biochem	"Hyperproliferative
				Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
				Chang and Karin, Nature	indications include boosting an
				410(6824):37-40 (2001); and	eosinophil-mediated immune
				Cobb MH, Prog Biophys Mol	response, and suppressing an
				Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune

response.																														
the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are important in	the late stage of allergic	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;
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				c					in	pa			£.	Z				ıts		its		Preferred indications	1 include neoplastic diseases		"Hyperproliferative	Disorders"), blood disorders	(e.g., as described below under	"Immune Activity",	"Cardiovascular Disorders",	-
Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999	Sep;104(3 Pt 1):565-74; and,	Sousa AR, et al., "In vivo	resistance to corticosteroids in	bronchial asthma is associated	with enhanced	phosyphorylation of JUN N-	terminal kinase and failure of	prednisolone to inhibit JUN N-	terminal kinase	phosphorylation" J Allergy	Clin Immunol; Sep;104(3 Pt	1):565-74 (1999); the contents	of each of which are herein	incorporated by reference in its	entirety.	Assays for the activation of	transcription through the AP1	response element are known in	the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	onto cominto of the
																						Activation of	transcription	through AP1	response element in	immune cells (such	as T-cells).			
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																						HLYBD32						,,		
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The state of the s	modulate growth and other cell	Disorders"), and infection
 	functions. Exemplary assays	(e.g., an infectious disease as
	for transcription through the	described below under
	AP1 response element that	"Infectious Disease"). Highly
	may be used or routinely	preferred indications include
	modified to test AP1-response	autoimmune diseases (e.g.,
	element activity of	rheumatoid arthritis, systemic
	polypeptides of the invention	lupus erythematosis, multiple
	(including antibodies and	sclerosis and/or as described
	agonists or antagonists of the	below) and
	invention) include assays	immunodeficiencies (e.g., as
	disclosed in Berger et al., Gene	described below). Additional
 	66:1-10 (1988); Cullen and	highly preferred indications
	Malm, Methods in Enzymol	include inflammation and
	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	272(49):30806-30811 (1997);	lymphoma, and/or as described
	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,
	reference in its entirety.	lung, colon, pancreatic,
	Mouse T cells that may be	esophageal, stomach, brain,
	used according to these assays	liver, and urinary cancer. Other
	are publicly available (e.g.,	preferred indications include
	through the ATCC).	benign dysproliferative
	Exemplary mouse T cells that	disorders and pre-neoplastic

may be used according to these assays include the HT2 cell line, which is an IL-2 metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	e assays, -3 assays, ulate and cell own in the or o assess otides of ing sts or vention) to
may be use assays incline, which dependent cell line that IL-4.	Activation of Adipocyte PI3 Kinase Signalling for PI3 kinase signal transduction that reg glucose metabolism survival are well-kno art and may be used routinely modified to the invention (includ antibodies and agoni antagonists of the invention include promote or inhibit gl
	HLYES38 1272
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	metabolism and cell survival.	of the invention includes a
	Exemplary assays for PI3	method for inhibiting
	kinase activity that may be	adipocyte proliferation. A
	used or routinely modified to	preferred embodiment of the
	test PI3 kinase-induced activity	invention includes a method
	of polypeptides of the	for stimulating adipocyte
	invention (including antibodies	differentiation. An alternative
	and agonists or antagonists of	highly preferred embodiment
	the invention) include assays	of the invention includes a
	disclosed in Forrer et al., Biol	method for inhibiting
	Chem 379(8-9):1101-1110	adipocyte differentiation.
	(1998); Nikoulina et al.,	Highly preferred indications
	Diabetes 49(2):263-271	include endocrine disorders
-	(2000); and Schreyer et al.,	(e.g., as described below under
	Diabetes 48(8):1662-1666	"Endocrine Disorders").
	(1999), the contents of each of	Preferred indications include
	which are herein incorporated	neoplastic diseases (e.g.,
	by reference in its entirety.	lipomas, liposarcomas, and/or
	Mouse adipocyte cells that	as described below under
	may be used according to these	"Hyperproliferative
	assays are publicly available	Disorders"), blood disorders
	(e.g., through the ATCC).	(e.g., hypertension, congestive
	Exemplary mouse adipocyte	heart failure, blood vessel
	cells that may be used	blockage, heart disease, stroke,
	according to these assays	impotence and/or as described
	include 3T3-L1 cells. 3T3-L1	below under "Immune
	is an adherent mouse	Activity", "Cardiovascular
	preadipocyte cell line that is a	Disorders", and/or "Blood-
	continous substrain of 3T3	Related Disorders"), immune
	fibroblast cells developed	disorders (e.g., as described
	through clonal isolation and	below under "Immune

heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.
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Additional highly preferred indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Highly preferred	indications include neoplasms	and cancer, such as, lipoma,	liposarcoma, lymphoma,	leukemia and breast, colon,	and kidney cancer. Additional	highly preferred indications	include melanoma, prostate,	lung, pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	
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		107																											1272
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324			cell 2B9		
324	HLYES38	1272	TNFa in Human T-cell 2B9		
	HMADS41	1273	Protection from	Caspase Apoptosis Rescue.	A highly preferred
325			Endothelial Cell	Assays for caspase apoptosis	embodiment of the invention
			Apoptosis.	rescue are well known in the	includes a method for
_				art and may be used or	stimulating endothelial cell
				routinely modified to assess	growth. An alternative highly
• 41				the ability of the polypeptides	preferred embodiment of the
				of the invention (including	invention includes a method
				antibodies and agonists or	for inhibiting endothelial cell
		•		antagonists of the invention) to	growth. A highly preferred
				inhibit caspase protease-	embodiment of the invention
				mediated apoptosis.	includes a method for
				Exemplary assays for caspase	stimulating endothelial cell
				apoptosis that may be used or	proliferation. An alternative
				routinely modified to test	highly preferred embodiment
				caspase apoptosis rescue of	of the invention includes a
				polypeptides of the invention	method for inhibiting
				(including antibodies and	endothelial cell proliferation.
		,		agonists or antagonists of the	A highly preferred
	_			invention) include the assays	embodiment of the invention
				disclosed in Romeo et al.,	includes a method for
				Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
				(2000); Messmer et al., Br J	growth. An alternative highly
			-	Pharmacol 127(7): 1633-1640	preferred embodiment of the
				(1999); and J Atheroscler	invention includes a method
				Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
				the contents of each of which	growth. A highly preferred
				are herein incorporated by	embodiment of the invention
			- Annual	reference in its entirety.	includes a method for

stimulating apoptosis of endothelial cells. An	alternative nighly preferred embodiment of the invention includes a method for	inhibiting (e.g., decreasing) apoptosis of endothelial cells.	A highly preferred embodiment of the invention	includes a method for stimulating angiogenisis. An	alternative highly preferred embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	highly preferred embodiment	of the invention includes a	hypertrophy. Highly preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive
Endothelial cells that may be used according to these assays	are publicly available (e.g., through commercial sources). Exemplary endothelial cells	that may be used according to these assays include bovine	aortic endothelial cells (bAEC), which are an example	of endothelial cells which line blood vessels and are involved	in functions that include, but are not limited to.	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.											
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Tankamiae and Kanoei''e	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	
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			 disease and Reynaud"s
			phenomenom, aneurysms,
			restenosis; venous and
			lymphatic disorders such as
			thrombophlebitis,
			lymphangitis, and
			lymphedema; and other
			vascular disorders such as
	<del></del>	-	peripheral vascular disease,
			and cancer. Highly
			preferred indications also
			include trauma such as
			wounds, burns, and injured
			tissue (e.g., vascular injury
			such as, injury resulting from
			balloon angioplasty, and
			atheroschlerotic lesions),
			implant fixation, scarring,
			ischemia reperfusion injury,
			rheumatoid arthritis,
		-	cerebrovascular disease, renal
-			diseases such as acute renal
			failure, and osteoporosis.
			Additional highly preferred
			indications include stroke,
			graft rejection, diabetic or
			other retinopathies, thrombotic
			and coagulative disorders,
			vascularitis, lymph
			angiogenesis, sexual disorders,
		10.1	age-related macular

degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic	inflammatory diseases, e.g.,	inflammatory bowel disease	and Crohn's disease), and pain	management.	A highly preferred
																												•		Kinase assay. Kinase assays,
	-									•••														***						Activation of
																														1273
													11 3/2						<u></u>				<u></u>							HMADS41
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	Tripatory to Triva	tot evalupte an Ein-1 nillase	
	Signaling Pathway	assay, tor EKK signal	includes a method for
-		transduction that regulate cell	stimulating hepatocyte cell
		proliferation or differentiation	proliferation. An alternative
		are well known in the art and	highly preferred embodiment
		may be used or routinely	of the invention includes a
		modified to assess the ability	method for inhibiting
		of polypeptides of the	hepatocyte cell proliferation.
		invention (including antibodies	A highly preferred
		and agonists or antagonists of	embodiment of the invention
		the invention) to promote or	includes a method for
		inhibit cell proliferation,	stimulating hepatocyte cell
		activation, and differentiation.	differentiation. An alternative
-		Exemplary assays for ERK	highly preferred embodiment
		kinase activity that may be	of the invention includes a
199		used or routinely modified to	method for inhibiting
		test ERK kinase-induced	hepatocyte cell differentiation.
		activity of polypeptides of the	A highly preferred
		invention (including antibodies	embodiment of the invention
		and agonists or antagonists of	includes a method for
		the invention) include the	activating hepatocyte cells. An
		assays disclosed in Forrer et	alternative highly preferred
		al., Biol Chem 379(8-9):1101-	embodiment of the invention
		1110 (1998); Kyriakis JM,	includes a method for
		Biochem Soc Symp 64:29-48	inhibiting the activation of
		(1999); Chang and Karin,	and/or inactivating hepatocyte
		Nature 410(6824):37-40	cells. Highly preferred
		(2001); and Cobb MH, Prog	indications include disorders of
		Biophys Mol Biol 71(3-4):479-	the liver and/or endocrine
		500 (1999); the contents of	disorders (e.g., as described
		each of which are herein	below under "Endocrine

	incorporated by reference in its	Disorders"). Preferred
	entirety Pot liver henotomo	-
	cillicty. Nat livel liepatolila	illulcations include neophasuc
	cells that may be used	diseases (e.g., as described
	according to these assays are	below under
	publicly available (e.g.,	"Hyperproliferative
	through the ATCC).	Disorders"), blood disorders
	Exemplary rat liver hepatoma	(e.g., as described below under
	cells that may be used	"Immune Activity",
	according to these assays	"Cardiovascular Disorders",
	include H4lle cells, which are	and/or "Blood-Related
	known to respond to	Disorders"), immune disorders
	glucocorticoids, insulin, or	(e.g., as described below under
	cAMP derivatives.	"Immune Activity"), neural
		disorders (e.g., as described
		below under "Neural Activity
		and Neurological Diseases"),
 		and infection (e.g., as
		described below under
		"Infectious Disease").
		A highly preferred indication
		is diabetes mellitus. An
		additional highly preferred
		indication is a complication
		associated with diabetes (e.g.,
		diabetic retinopathy, diabetic
		nephropathy, kidney disease
		(e.g., renal failure,
		nephropathy and/or other
		diseases and disorders as
		described in the "Renal".
		Disorders" section below),

diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal
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tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly	preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred indications include, hepatitis, jaundice, gallstones, cirrhosis	or the liver, degenerative or necrotic liver disease, alcoholic liver diseases, fibrosis, liver regeneration, metabolic disease, dyslipidemia and chlolesterol metabolism.  Additional highly preferred indications include neoplasms and cancers, such as,

hepatocarcinomas, other liver cancers, and colon and pancreatic cancer. Preferred indications also include prostate, breast, lung, esophageal, stomach, brain, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia.	lys for Preferred embodiments of the invention include using polypeptides of the invention d to (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.  Mast tive lighout tion
	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues throughout the body, and their activation via immunoglobulin E-antigen, promoted by T helper cell tyne 2 cytokines is an
	Regulation of apoptosis of immune cells (such as mast cells).
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	HMADS41
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important component of allergic disease. Dysregulation of mast cell apoptosis may play a role in allergic disease and mast cell tumor survival.	Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity	induced by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the	assays disclosed in: Masuda A, et al., J Biol Chem, 276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103 (2000);Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are	herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g.,	through commercial sources).
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may be used according to these assays include mast cells such as the HMC human mast cell line.	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 production and increases light production and increases light production and increases light production and increases lightly preferred embodiment of the invention includes a nethod for inhibiting (e.g., increasing) IL-6 production. An alternative lightly preferred embodiment of the invention of the invention of the invention includes a method for inhibiting (e.g., increasing) IL-6 production. An alternative lightly preferred embodiment of the invention of the invention of the invention includes a method for inhibiting (e.g., increasing) IL-6 production. An alternative lightly preferred embodiment of the invention of the invention of the invention of the invention includes a method for inhibiting (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention of the invention of the invention includes a method for inhibiting (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., increasing) IL-6 production. An alternative highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly proteins produced by a large variety of cells where the saperssion level is strongly and described below under whom in the art and may be described below under whom in the art and may be assess the ability of autoimmune diseases (e.g., as described below under whom in the art and may be alto more assess the ability of autoimmune diseases (e.g., as described below under whom in the art and may be alto more assess the ability of autoimmune diseases (e.g., as deferted indications include autoimmune diseases (e.g., as described below under whom in the art and may be alto more assess the ability of autoimmune diseases (e.g., as deferted indications include autoimmune diseases (e.g., as described below under whom in the art and may be alto more and and infection (e.g., as described below under and may be alto more and and
	Production of IL-6
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	inventi	invention) to mediate	below) and
	unmui	immunomodulation and	immunodeficiencies (e.g., as
	differen	differentiation and modulate T	described below). Highly
	cell pro	cell proliferation and function.	preferred indications also
	Exemp	Exemplary assays that test for	include boosting a B cell-
	immun	immunomodulatory proteins	mediated immune response
	evaluat	evaluate the production of	and alternatively suppressing a
	cytokin	cytokines, such as IL-6, and	B cell-mediated immune
	the stin	the stimulation and	response. Highly preferred
	nbregu	upregulation of T cell	indications include
-	prolife	proliferation and functional	inflammation and
	activiti	activities. Such assays that	inflammatory
	may be	may be used or routinely	disorders.Additional highly
	finodifie	modified to test	preferred indications include
	unuui	immunomodulatory and	asthma and allergy. Highly
	difffere	diffferentiation activity of	preferred indications include
	polype	polypeptides of the invention	neoplastic diseases (e.g.,
	(includ	(including antibodies and	myeloma, plasmacytoma,
	agonist agonist	agonists or antagonists of the	leukemia, lymphoma,
	inventi	invention) include assays	melanoma, and/or as described
	disclos	disclosed in Miraglia et al., J	below under
	Biomo	Biomolecular Screening 4:193-	"Hyperproliferative
	204(19	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymb	"Lymphocytes: a practical	indications include neoplasms
-	approa	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000)	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	unwul   Immuu	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997)	(1997), the contents of each of	prostate, breast, lung, colon,
	which	which are herein incorporated	pancreatic, esophageal,
	by refe	by reference in its entirety.	stomach, brain, liver and
	Humar	n dendritic cells that may	Human dendritic cells that may   urinary cancer. Other preferred

				be used according to these	indications include benign
				assays may be isolated using	dysproliferative disorders and
				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
		· · · · · · · · · · · · · · · · · · ·			granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
			-		organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
		1991			meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HMADU73	1274	Production of TNF	TNFa FMAT. Assays for	A highly preferred
326			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
-			cells	produced by activated	includes a method for
	_			macrophages, T cells,	inhibiting (e.g., decreasing)
				- www.	

fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J	scle TNF alpha production An	rt a		na includes a method for	known stimulating (e.g., increasing)		_	des of   include blood disorders (e.g.,		or   "Immune Activity", "Blood-			and Highly preferred indications		(e.g., rheumatoid arthritis,				NFa), below), immunodeficiencies		boosting a T cell-mediated	ch immune response, and	l or suppressing a T cell-mediated	st immune response. Additional		ention   include inflammation and	nd inflammatory disorders, and		ys patients with rheumatoid	al., J arthritis. An additional highly	4.102   moformed indication is some
	fibroblasts smooth mit	and other cell types tha	wide variety of inflamn	and cytotoxic effects on a	variety of cells are well known	in the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists	antagonists of the inver	mediate immunomodulation,	modulate inflammation and	cytotoxicity. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or	cytotoxic response. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Riomologillar Corsoning 1.103

		204(1999); Rowland et al.,	Highly preferred indications
		"Lymphocytes: a practical	include neoplastic diseases
		approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
		(2000); Verhasselt et al., Eur J	and/or as described below
		Immunol 28(11):3886-3890	under "Hyperproliferative
	_	(1198); Dahlen et al., J	Disorders"). Additionally,
		Immunol 160(7):3585-3593	highly preferred indications
		(1998); Verhasselt et al., J	include neoplasms and
		Immunol 158:2919-2925	cancers, such as, leukemia,
		(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
		Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
		(1999), the contents of each of	tumors, and prostate, breast,
		which are herein incorporated	lung, colon, pancreatic,
		by reference in its entirety.	esophageal, stomach, brain,
71		Human dendritic cells that may	liver and urinary cancer. Other
		be used according to these	preferred indications include
		assays may be isolated using	benign dysproliferative
		techniques disclosed herein or	disorders and pre-neoplastic
		otherwise known in the art.	conditions, such as, for
		Human dendritic cells are	example, hyperplasia,
		antigen presenting cells in	metaplasia, and/or dysplasia.
		suspension culture, which,	Preferred indications include
		when activated by antigen	anemia, pancytopenia,
		and/or cytokines, initiate and	leukopenia, thrombocytopenia,
		upregulate T cell proliferation	Hodgkin's disease, acute
		and functional activities.	lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
			disease, inflammatory bowel
			disease, neutropenia,

neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").			Assays for production of IL-10 Highly preferred indications and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to and activation of T-cells. Exemplary assays that may be used or routinely modified to and activation of T-cells. In the allity of a secrept and activation of T-cells. In the art and may be include allergy and asthma.  Additional highly preferred include immune and hematopoietic disorders and hematopoietic disorders (e.g., as described below under "Blood-Related Disorders"), autoimmune diseases (e.g., inhibit production of IL-10 lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immune diseases (e.g., inhibit production of T-cells.
	nB	man T	
	IgG in Human B cells SAC	CD152 in Human T cells	Production of IL-10 and activation of T-cells.
	1274	1274	1274
	HMADU73	HMADU73	HMADU73
	326	326	326

ies of described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune			-2 see"	896	-1.		utics;		are			be	ssays	lay be	Th2	s are	ete	IL6.		ion	r role	
polypeptides and antibodies of the invention (including agonists or antagonists of the invention) to modulate II-10	production and/or T-cell proliferation include, for	example, assays such as disclosed and/or cited in:	Robinson, DS, et al., "Th-2 cytokines in allergic disease."	Br Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	neiper type z cell-directed therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary cells that may be	used accoloning to these assays include Th2 cells. II.10	secreted from Th2 cells may be	measured as a marker of Th2	cell activation. Th2 cells are	a class of T cells that secrete	IL4, IL10, IL13, IL5 and IL6.	Factors that induce	differentiation and activation	of Th2 cells play a major role	in the initiation and
														149								

o	an cause   (e.g., due to diadence   neuropathy), blood vessel   sading to   blockage, heart disease, stroke,			confusion, drowsiness, nonketotic hyperglycemic-	hyperosmolar coma, cardiovascular disease (e.g
/ and / and in vitro in vitro rizing neral lated lated calcium the art utinely ability ability ability ize ed to um. rry low solic nuch	an cause	3 8			
pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.  Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium.  Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium	Extracellular factors can cause an influx of calcium, leading to	activation of calcium activation efendam	responsive signating pathways and alterations in cell	functions. Exemplary assays that may be used or routinely	modified to measure calcium flux by polypeptides of the
Stimulation of Calcium Flux in pancreatic beta cells.					
1275					
HMAMI15					
327					

invention (including antibodies	heart disease, atherosclerosis,
and agonists or antagonists of	microvascular disease,
 the invention) include assays	hypertension, stroke, and other
disclosed in: Satin LS, et al.,	diseases and disorders as
Endocrinology, 136(10):4589-	described in the
601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
Endocrinology, 136(7):2960-6	section below), dyslipidemia,
(1995); Richardson SB, et al.,	endocrine disorders (as
Biochem J, 288 ( Pt 3):847-51	described in the "Endocrine
(1992); and, Meats, JE, et al.,	Disorders" section below),
Cell Calcium 1989 Nov-	neuropathy, vision impairment
Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
 contents of each of which is	blindness), ulcers and impaired
herein incorporated by	wound healing, and infection
reference in its entirety.	(e.g., infectious diseases and
Pancreatic cells that may be	disorders as described in the
used according to these assays	"Infectious Diseases" section
are publicly available (e.g.,	below, especially of the
through the ATCC) and/or	urinary tract and skin), carpal
 may be routinely generated.	tunnel syndrome and
 Exemplary pancreatic cells that	Dupuytren's contracture).
may be used according to these	An additional highly preferred
assays include HITT15 Cells.	indication is obesity and/or
HITT15 are an adherent	complications associated with
epithelial cell line established	obesity. Additional highly
from Syrian hamster islet cells	preferred indications include
transformed with SV40. These	weight loss or alternatively,
cells express glucagon,	weight gain. Aditional
somatostatin, and	highly preferred indications are
glucocorticoid receptors. The	complications associated with
cells secrete insulin, which is	insulin resistance.

stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.		Assays for activation of transcription are well-known in the art and may be used and routinely modified to assess ability of polypeptides of the invention to inhibit or activate transcription. An example of such an assay follows: Cells were pretreated with SID supernatants or controls for 15-18 hours. SEAP activity was measured after 48 hours.  LS174T is an epithelial colon adenocarcinoma cell line. Its tumourigenicity in nude mice make cell line LS174T a model for studies on the mechanism of synthesis and secretion of specific tumoral markers in colon cancer. See, Patan et al.,
	CD152 in Human T cells	Activation of Transcription
	1275	1275
	HMAMI15	HMAMI15
	327	327

				Circ Res, 89(8):732-39 (2001), the contents of which are	
				herein incorporated by	
				reference in its entirety.	
	HMDAE65	1276	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
328				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
	.,,,,			IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
	200			expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,
	-			polypeptides of the invention	rheumatoid arthritis, systemic
				(including antibodies and	lupus erythematosis, multiple
				agonists or antagonists of the	sclerosis and/or as described
				invention) to mediate	below) and

			immunomodulation and	immunodeficiencies (e.g., as
			differentiation and modulate T	described below). Highly
			cell proliferation and function.	preferred indications also
			Exemplary assays that test for	include boosting a B cell-
			immunomodulatory proteins	mediated immune response
			evaluate the production of	and alternatively suppressing a
	<u></u>		cytokines, such as IL-6, and	B cell-mediated immune
			the stimulation and	response. Highly preferred
			upregulation of T cell	indications include
			proliferation and functional	inflammation and
-			activities. Such assays that	inflammatory
			may be used or routinely	disorders.Additional highly
-			modified to test	preferred indications include
			immunomodulatory and	asthma and allergy. Highly
			diffferentiation activity of	preferred indications include
	-		polypeptides of the invention	neoplastic diseases (e.g.,
			(including antibodies and	myeloma, plasmacytoma,
			agonists or antagonists of the	leukemia, lymphoma,
			invention) include assays	melanoma, and/or as described
			disclosed in Miraglia et al., J	below under
			Biomolecular Screening 4:193-	"Hyperproliferative
			204(1999); Rowland et al.,	Disorders"). Highly preferred
			"Lymphocytes: a practical	indications include neoplasms
			approach" Chapter 6:138-160	and cancers, such as, myeloma,
			(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
			Immunol 158:2919-2925	lymphoma, melanoma, and
	,		(1997), the contents of each of	prostate, breast, lung, colon,
	-		which are herein incorporated	pancreatic, esophageal,
			by reference in its entirety.	stomach, brain, liver and
			Human dendritic cells that may	urinary cancer. Other preferred
			be used according to these	indications include benign

			Griron manning on faire a facon	
			techniques disclosed herein or	pre-neoplastic conditions, such
			otherwise known in the art.	as, for example, hyperplasia,
_			Human dendritic cells are	metaplasia, and/or dysplasia.
	_		antigen presenting cells in	Preferred indications include
			suspension culture, which,	anemia, pancytopenia,
			when activated by antigen	leukopenia, thrombocytopenia,
			and/or cytokines, initiate and	Hodgkin's disease, acute
			upregulate T cell proliferation	lymphocytic anemia (ALL),
			and functional activities.	multiple myeloma, Burkitt's
				lymphoma, arthritis, AIDS,
				granulomatous disease,
		,		inflammatory bowel disease,
			4	sepsis, neutropenia,
			,	neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
_				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, and Lyme Disease.
				An additonal preferred
				indication is infection (e.g., an
				infectious disease as described
	4			below under "Infectious
				Disease").
HMDAM24	1277	Protection from	Caspase Apoptosis Rescue.	A highly preferred
		Endothelial Cell	Assays for caspase apoptosis	embodiment of the invention
	****	Apoptosis.	rescue are well known in the	includes a method for
			art and may be used or	stimulating endothelial cell
			routinely modified to assess	growth. An alternative highly